*Critical Care* Volume 9 Suppl 1, 2005

# 25th International Symposium on Intensive Care and Emergency Medicine

Brussels, Belgium, 21–25 March 2005

Published online: 7 March 2005
These abstracts are online at http://ccforum.com/supplements/9/S1


## P1

### Severe community-acquired pneumonia in the intensive care unit

**C Costa, I Gouveia, P Cunha, R Milheiro, A Bártolo, C Gonçalves, A Carvalho, T Cardoso, S Martins, J Magalhães**
*HSO, Guimarães, Portugal*
*Critical Care* 2005, **9(Suppl 1):**P1 (DOI 10.1186/cc3064)

**Introduction** Community-acquired pneumonia remains a common condition worldwide. It is associated with significant morbidity and mortality. The aim of this study was to evaluate conditions that could predict a poor outcome.
**Design** Retrospective analyse of 69 patients admitted to the ICU from 1996 to 2003. Demographic data included age, sex and medical history. Etiologic agents, multiorgan dysfunction, nosocomial infections, SAPS II and PORT scores were recorded for each patient. For statistical analysis we used a *t* test, chi-square test and Mann–Whitney U test on SPSS®. A value of *P* less than 0.05 was considered significant.
**Results** Forty-seven patients were male and 22 patients were female. Mean age was 52 years. Sixty-seven percent had serious pre-morbid conditions including pulmonary disease (34.8%), cardiac problems (36.2%), diabetes (13%) and chronic liver disease (5.8%); 40.6% were smokers, drug abusers or alcohol dependents. Sixty-eight patients required invasive mechanical ventilation. The average length of ventilation was 13.5 days, median 8 days. The mean SAPS II score was 40.14 and the mean PORT score was 141. The mortality rate was 27.5% (SAPS II estimated mortality, 35%). Complications reported were ARDS (40.6%), septic shock (34.8%), acute renal failure (2.9%), cardiac arrest (8.7%) and nosocomial infeccions (46.4%). Mortality rates were higher for previous hepatic (75%) and metabolic (33%) diseases. We found a close association between crude mortality and SAPS II score ($P = 0.003$) and development of complications ($P = 0.0028$). Respiratory dysfunction ($P = 0.006$) and septic shock ($P = 0.022$) were most significantly related to mortality. No significant differences were founded regarding age, comorbidities, PORT score, etiologic agents, nosocomial infections and length of invasive mechanical ventilation.
**Conclusions** Previous hepatic chronic disease was strictly related to higher mortality as well as isolation of MRSA. ARDS and septic shock predicted a poor outcome. SAPS II score was the best severity indicator of mortality.

## P2

### Closed endotracheal suction system without periodic change versus open endotracheal system

**L Lorente, M Lecuona, J Villegas, M Mora, A Sierra**
*Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain*
*Critical Care* 2005, **9(Suppl 1):**P2 (DOI 10.1186/cc3065)

**Objective** It is known that the closed tracheal suction system (CTSS) produces less hemodynamic and gasometric deterioration than an open tracheal suction system (OTSS). Use is limited because no decrease in the incidence of ventilator-associated pneumonia (VAP) was found and also because it is more expensive. But, is daily periodic change of the CTSS necessary? The aim of this study was to analyze the incidence of VAP using a CTSS without periodic change versus an OTSS.
**Methods** It is a prospective study of ICU patients from 1 January 2004 to 31 October 2004. Patients who required mechanical ventilation (MV) were randomized into two groups: one group was suctioned with CTSS without periodic change and another group with OTSS. An aspirate tracheal swab and a throat swab on admission and afterwards twice weekly were taken. VAP was classified based on throat flora in endogenous and exogenous samples. The statistical analysis was performed by chi-square test and Student's *t* test, and we took $P < 0.05$ as a significant difference.
**Results** There were no significant differences between both groups of patients (236 with CTSS without periodic change and 211 with OTSS) in age, sex, diagnosis groups, APACHE II score, number of aspirations per day and mortality. No significant differences were found in the percentage of patients who developed VAP (13.98% vs 14.02%), nor in the number of VAP per 1000 MV-days (14.13 vs 14.67). At the same time we did not find any differences in the percentage of patients who developed exogenous VAP (0.96% vs 0.88%). In the patients who needed MV during 24 hours or more, the aspiration cost was less expensive in the CTSS without periodic change group than in the OTSS group ($1.89 × 1.53 vs $2.45 × 0.71 per patient-day, $P < 0.0001$).
**Conclusions** We conclude that in our study the CTSS without periodic change decreased the aspiration cost and did not modify the VAP incidence.

## P3

### Ventilator-associated pneumonia caused by multidrug resistant bacteria

**M Sartzi, M Charitidou, A Panagiotakopoulou, C Michas, F Tsidemiadou, P Clouva-Molyvdas**
*'THRIASSIO' Hospital of Eleusis, Attica, Greece*
*Critical Care* 2005, **9(Suppl 1):**P3 (DOI 10.1186/cc3066)

**Introduction** The aim of the study was to investigate the epidemiology, clinical characteristics and severity of ventilator-associated pneumonia (VAP) caused by multidrug resistant bacteria (Group I) and to identify possible differences from VAP caused by sensitive pathogens (Group II).
**Methods** A prospective observational 2-year study of all ICU patients who developed VAP. Age, gender, APACHE II score, underlying disease, cause of ICU admittance, length of ICU stay, duration of mechanical ventilation (MV) before the onset of VAP and total duration of MV, VAP pathogens, day of VAP onset and patient outcome were recorded. The Multi Organ Dysfunction Score (MODS) and Clinical Pulmonary Index Score (CPIS) were measured at the onset of VAP. Statistical evaluation was

performed using the nonparametric Mann–Whitney test and Pearson's chi test.

**Results** During this 2-year period 240 patients were admitted to the ICU. Fifty patients (20.8%) developed VAP. All VAP was late onset. VAP was caused by multidrug resistant pathogens in 23 patients (Group I) and by sensitive bacteria in 27 patients (Group II). ICU admittance ($P = 0.27$), underlying disease ($P = 0.83$) and type of isolated bacteria ($P = 0.53$) did not differ between the two groups. All the other results are presented in Table 1.

**Table 1**

| | Group I ($n = 23$) | Group II ($n = 27$) | $P$ value |
|---|---|---|---|
| Men/women | 17/6 | 21/6 | 0.75[c] |
| Age | 59.8 ± 18.0[a] | 60.7 ± 21.4[a] | 0.6[b] |
| APACHE II score | 20 (CI: 17.5–22.5) | 21.1 (CI: 18.3–24) | 0.71[b] |
| Outcome (deaths) | 8 (34.8%) | 4 (14.8%) | 0.09[c] |
| CPIS | 6.8 (CI: 6.6–7.0) | 6.3 (CI: 6.1–6.6) | 0.003[b] |
| MODS | 8.9 (CI: 7.9–9.8) | 4.6 (CI: 3.9–5.2) | 0.0001[b] |
| Days of MV before VAP | 16.1 ± 10.1[a] | 17.8 ± 10.1[a] | 0.11[b] |
| Total days of MV | 40.1 ± 18.1[a] | 36.7 ± 22.0[a] | 0.37[b] |
| LOS in ICU | 46 ± 21.2[a] | 39.9 ± 23.9[a] | 0.26[b] |

LOS, length of stay; CPIS, Clinical Pulmonary Index Score; MODS, Multi Organ Dysfunction Score; MV, mechanical ventilation; CI, 95% confidence interval. [a]Data presented as mean ± standard deviation. [b]Mann–Whitney test. [c]Pearson's chi test.

**Conclusions** Patients that developed VAP due to multiresistant bacteria did not differ in their basic characteristics (age, gender, APACHE II score, underlying disease and cause of admittance) from patients that developed VAP due to sensitive strains. However, MODS and CPIS at the onset of VAP were significantly higher in patients with VAP caused by multiresistant bacteria. The difference in outcome between the two groups, although not statistically significant, may have reached significance if our sample was larger.

## P4

## Ventilator-associated pneumonia and Clinical Pulmonary Infection Score validation in a Greek general intensive care unit

**P Myrianthefs, K Ioannidis, M Mis, S Karatzas, G Baltopoulos**
*KAT Hospital, Athens, Greece*
*Critical Care* 2005, **9(Suppl 1):**P4 (DOI 10.1186/cc3067)

**Background** Ventilator-associated pneumonia (VAP) is a significant clinical problem in the ICUs and accurate diagnosis remains problematic. The purpose of the study was to examine the characteristics of VAP in a general Greek ICU.

**Methods** We prospectively recorded the characteristics of VAP for a period of 5 months in a seven-bed ICU. We collected 1032 ventilator days (VD) concerning 64 patients admitted to our ICU. Data collected included demographics, VAP episodes, pathogens, resistance characteristics and outcomes. We also validated the Clinical Pulmonary Infection Score (CPIS) as a guide for VAP diagnosis [1]. We defined VAP as having CPIS ≥ 6.

**Results** We included 64 patients admitted to our ICU (43 men) of mean age 50.8 ± 4.6 years. Patients were admitted from the emergency department, wards, other ICUs and the operating room suffering from multiple trauma including head injury (25), stroke (14), postoperative respiratory failure (10), heart failure (seven), sepsis (five), and other medical conditions (three). We recorded 1032 VD. Twenty-one patients (21/64, 32.8%) developed VAP. Four patients developed two separate episodes of VAP. We in total recorded 25 episodes of VAP. The incidence of VAP was 24.2 episodes per 1000 VD. The duration of VAP until resolution was 11.4 ± 0.9 days. The total duration of mechanical ventilation (MV) was 29.7 ± 5.3 days and the mean duration of MV before the development of VAP was 19.9 ± 4.8 days.

We identified multidrug resistant pathogens (*Acinetobacter baumanii*) in two patients and one of them died due to VAP. We also identified pathogens sensitive only to colistin (*A. baumanii* in eight patients and *Pseudomonas aeruginosa* in two patients) in 10 patients, five of them died and one of them died due to VAP (Table 1).

**Table 1**

| | |
|---|---|
| Gram(–) | 16/25 (65%) |
| *Acinetobacter baumanii* | 12 |
| *Pseudomonas aeruginosa* | 4 |
| Mixed | 9/25 (35%) |
| *A. baumanii* + *P. aeruginosa* | 5 |
| *A. baumanii* + *Staphylococcus aureus* | 2 |
| *A. baumanii* + fungi | 1 |
| *Klebsiella pneumoniae* + fungi | 1 |

The VAP-attributable mortality was 23.8% (5/21). VAP was successfully resolved in 20/25 episodes. Management of VAP was guided according to culture results and in the case of multidrug resistance or single antibiotic sensitivity by the use of combination antibiotic therapy including meropenem, high-dose ampicillin-sulbactam and collistin.

CPIS sensitivity was 82.7%, specificity was 89.2%, positive predictive value was 73.2% and negative predictive value was 93.5%.

**Conclusions** VAP significantly contributes to morbidity and mortality of critically ill ICU patients. However, VAP may be successfully treated even in the case of multidrug resistance or single antibiotic sensitivity by combination therapy. CPIS may be a significant tool in the diagnosis of VAP in our ICU.

**Reference**

1. Singh N, *et al.*: *Am J Respir Crit Care Med* 2000, **162:**505-511.

## P5

## Ventilator-associated pneumonia in neuromuscular, tracheostomyzed patients

**A Martini, N Menestrina, E Mantovani, B Allegranzi, G Finco, L Gottin**
*Ops Poloclinico GB Rossi, Verona, Italy*
*Critical Care* 2005, **9(Suppl 1):**P5 (DOI 10.1186/cc3068)

**Objective** Lower-tract respiratory infections are common events in tracheostomyzed mechanically ventilated patients leading to a 10-fold increase in mortality rate particularly in those patients with severely compromized clinical conditions [1]. Our study aimed to assess epidemiology and risk factors for colonization of respiratory tract and development of ventilator-associated pneumonia (VAP) in home-living, tracheostomyzed and mechanically ventilated patients with neuromuscular disease.

**Design** A retrospective study.

**Setting** An ICU ambulatorial service for neuromuscular disease.

**Patients** Data of 27 patients (20 male) that underwent a routine visit every 6 months, collected from 1995 until 2003, were analyzed. Thirteen had amyotrophic lateral sclerosis (ALS) and one spinal muscular atrophy (ALS-like group); seven had Duchenne's dystrophy (DMP), two congenital dystrophy, three metabolic dystrophy and one supranuclear progressive paralysis (DMP-like group).

The median age was 54 years (interquartile range, 31–63). The median mechanical ventilation period (MVP) was 71 months (30–120).

Thirteen patients had severe dysphagy and ineffective cough reflex, 12 of them were alimentated by percutaneous enteral gastrostomy and one by nasal-gastric tube, ALS-like patients were more frequently dysphagic than DMP-like patients ($P < 0.01$).

Low respiratory tract infections (LRTI) were defined in the presence of cough or an abnormal increase of bronchial secretions, with or without fever that required antibiotic therapy; pneumonia was defined as LRTI with a new pulmonary infiltrate at thorax radiography [2].

**Measurements and main results** VAP incidence was 52 episodes for 100 patients per year of MVP. The median MVP was lower in dysphagic patients (33 months [20.75–70.50]) than in non-dysphagic patients (120 months [80–156]) ($P < 0.01$) and in ALS-like patients (33 months [24–73]) than in the DMP-like group of patients (96 months [69.5–144]).

Dysphagic patients had an higher colonization incidence (Ci) ($P = 0.01$), LTRI incidence (LTRIi) ($P$ = not significant), and VAP incidence (VAPi) ($P = 0.02$) than nondysphagic patients, per month of mechanical ventilation.

ALS-like patients had a higher Ci and VAPi than DMP-like patients ($P$ = not significant).

Bivariate analysis shown a positive correlation between Ci and LTRIi and VAPi ($P < 0.01$ for both). MVP was negatively correlated with Ci ($P < 0.01$) and VAPi, although the $P$ value was 0.06. *Pseudomonas aeruginosa* was the most isolated bacteria in colonization (48%), LTRI (45%) and VAP (52%) episodes.

**Conclusion** VAP is a frequent event in our patients. Dysphagic patients, although alimentated by gastrostomy, are more frequently colonized and this enhances the risk to develop VAP more than in nondysphagic patients. Patients ventilated for a long period seem to develop a natural defence from colonization. The longer the MVP, the less the patient is prone to be colonized and, likely, to develop VAP. The risk of developing VAP is no different in ALS-like and DMP-like disease although the dysphagy prevalence differs. A bigger sample is needed to definitively prove this.

**References**

1. Niedermann MS, *et al.*: **Nutritional status and bacterial binding in the lower respiratory tract in patients with chronic tracheostomy.** *Ann Intern Med* 1972, **77:**701-706.
2. Harlid R, *et al.*: **Respiratory tract colonization and infection in patients with chronic tracheostomy.** *Am J Resp Critical Care* 1996, **154:**124-129.

## P6

## Clinical characteristics of ventilator-associated pneumonia patients and control patients

**M Moock, LL Maia, ALC Meserami, CM Broncher, JL Oliveira, SC Oliveira, JMO Orlando**
*ICU Hospital Geral de Pedreira, São Paulo, Brazil*
*Critical Care* 2005, **9(Suppl 1):**P6 (DOI 10.1186/cc3069)

**Introduction** Ventilator-associated pneumonia (VAP) represents 80% of all nosocomial pneumonia. The aim of this study is an epidemiological, performance and outcome evaluation of an ICU, focused in VAP.

**Methods** The study was performed in a 13-bed ICU located in São Paulo, Brazil, during 2003. It was a retrospective study, where all consecutive patients admitted were included. All data were collected and analysed in a Brazilian system of performance and quality in the ICU, called QuaTI®. Statistical analyses were done, supported by the EpiInfo 2002 software. Clinical characteristics of all patients were presented and then two groups were analysed and compared: VAP group ($n = 28$) and control group ($n = 231$) composed of ventilated patients who did not develop VAP.

**Results** From 11 January to 31 December, 483 patients were admitted; 55.69%, were male; median age was 59 years, 362 medical and 121 surgical patients; medium length of stay was 8.91 ± 13.07 days. APACHE II median score was 11.78 ± 7.13; mortality rate was 29.6% and standard mortality rate, calculated by APACHE II, was 1.01. The rate of ventilated patients was 259/483 (53.62%). The VAP incidence was 10.81% and the rate was 10.84 per 1000 ventilator days. The infection agent was identified in 15 patients by bronchoalveolar lavage or blood cultures. The more prevalent were *Pseudomonas aeuriginosa* (6/28), *Klebisiella pneumoniae* (2/28), *Staphylococcus aureus* (2/28).

**Table 1**

| Characteristics | VAP ($n = 28$) | Controls ($n = 231$) | $P$ value |
|---|---|---|---|
| Age (years), median | 57 | 66 | 0.10 |
| % male | 85.7 | 74 | 0.17 |
| Medical | 24 | 171 | 0.17 |
| Surgical | 4 | 60 | 0.17 |
| ICU stay (days) | 30.79 ± 18.06 | 12.25 ± 14.97 | 0.000 |
| Ventilation days | 27.61 ± 20.19 | 10.41 ± 13.21 | 0.000 |
| APACHE II score | 16.50 ± 5.77 | 13.96 ± 7.39 | 0.04 |
| Death risk (%) | 21.39 | 33.32 | 0.02 |
| Mortality rate (%) | 32.14 | 51.52 | 0.053 |

**Conclusions** VAP did not increase mortality but improved ventilated days, ICU length of stay and assistance costs. The APACHE II score was significantly higher in patients who developed VAP. *P. aeuriginosa* was the predominant pathogen.

**Reference**

Rello J: *Crit Care Med* 2003, **31:**2544-2551.

## P7

## Nosocomial pneumonia: impact of a very early antimicrobial therapy

**L Montesino, C Cazenave, X Jeusset, P Remi, M Thyrault, J Coudray**
*General Hospital of Longjumeau, France*
*Critical Care* 2005, **9(Suppl 1):**P7 (DOI 10.1186/cc3070)

**Introduction** Nosocomial pneumonia (NP) severely complicates the course of mechanical ventilation. Although the need of an appropriate antimicrobial therapy adapted from the results of cultures from lower respiratory samples is well known, the best moment to start it is yet to be defined.

**Objective** To assess the benefits of an appropriate antimicrobial therapy started just after the direct sample examination versus after the culture results.

**Design and patients** A retrospective cohort study including 50 NP cases, diagnosed on clinical examination, bronchoalveolar lavage and protected specimen brush. Once the radiological and clinical characteristics of the patient have been analysed, the antimicrobial therapy modality is studied. Patients have been separated into two groups, depending on the delay before the antimicrobial therapy: just after the direct examination for group 1 (G1) and after the culture analysis for group 2 (G2).

**Measurement and results** For G1 the appropriate antimicrobial therapy is started with a delay of 4.6 ± 2.5 hours after the direct examination results, while for G2 this delay reaches 34.5 ± 22.5 hours. Hence, in 44 patients, initial antimicrobial therapy was appropriate straightway and in the remaining six patients was adapted on the results of culture. No differences have been

noticed in terms of mortality (54% vs 53%, $P = 0.91$) and length of stay in the intensive care unit (28.7 days vs 19.3 days, $P = 0.16$) between the two groups. Both were similar regarding clinical and radiological diagnosis, age and severity of the NP. However, in G2, a significantly higher number of multi-resistant bacteria have been found (87% vs 73%, $P < 0.001$) as well as a higher rate of tracheal colonization within 48 hours after the fiberoptic bronchoscopy (76% vs 60%, $P < 0.001$).

**Conclusion** For patients having a NP of moderate gravity, it is possible to wait for the culture before the start of antimicrobial therapy.

## P8

### Antibiotics for preventing infections in open fractures are protective against ventilator-associated pneumonia

**F Cancellieri[1], G Gambale[1], M Baldazzi[2]**
*[1]Ospedale Maggiore, Bologna, Italy; [2]Universiità degli Studi, Bologna, Italy*
*Critical Care* 2005, **9(Suppl 1):**P8 (DOI 10.1186/cc3071)

**Introduction** Early ventilator-associated pneumonia (VAP) remains the commonest infection in ICUs, in trauma in particular. Controversy exists on whether antibiotic prophylaxis for traumatic lesions increases the respiratory infection rate and antibiotic resistance [1].

**Methods** Using the trauma registry and data from the infection surveillance program, we reviewed major trauma cases: admitted consecutively and directly to our unit in 4 years, with a stay longer than 3 days that received no antibiotic at all or received clindamycin-gentamicin from admission for open fractures. Statistical analysis consisted of: Fisher's exact test, Student's *t* test, multiple logistic regression.

**Results** Four hundred and eighty-two patients did not receive antibiotics, 126 did, for 2.8 ± 1.8 days. Groups were not statistically different in age, sex, injury severity score, Glasgow Coma Score (GCS) at admission, prehospital intubation rate, days of artificial ventilation and sedation, surgery, and transfusions. Bivariate analysis of the groups with and without VAP (272 vs 336) showed a statistically significant difference in injury severity score, GCS, days of ventilation, prehospital intubation and antibiotic treatment. Days of ventilation, anatomical severity of trauma and antibiotic treatment were independently associated with VAP in a logistic multivariate model. Antibiotics showed a protective effect against VAP: odds ratio, 0.386; 95% confidence interval, 0.227–0.657. VAP in non-antibiotic treated patients was caused by *Staphylococcus aureus* in 37.7% (4% methicillin-resistant *S. aureus* [MRSA]) of cases, haemophilus in 25%, Gram-negative, including pseudomonas, in 25.4%. In patients treated with antibiotics *S. aureus* was isolated in 17.4% of cases (5.5% MRSA), haemophilus in 30.4%, Gram-negative, including pseudomonas, in 43.1%.

**Table 1**

| Variable | *P* value | Odds ratio | 95% CI, lower | 95% CI, upper |
|---|---|---|---|---|
| Injury severity score | < 0.01 | 1.027 | 1.006 | 1.047 |
| Days on ventilator | < 0.0001 | 1.241 | 1.188 | 1.296 |
| Antibiotics yes/no | < 0.001 | 0.386 | 0.227 | 0.657 |

**Conclusion** Seventy-two hours of antibiotic therapy for open third-degree fracture is protective against VAP in trauma patients. When VAP occurs after or during antibiotic treatment, isolations shift towards haemophilus, pseudomonas or other Gram-negative germs, not MRSA.

### Reference

1. Hoth JJ: **Prophylactic antibiotics adversely affect nosocomial pneumonia in trauma patients.** *J Trauma* 2003, **55:**249-254.

## P9

### A simple program to reduce the incidence of ventilator-associated pneumonia in a Brazilian intensive care unit

**P Souza, M Lugarinho, A Martinez, L Felix**
*Hospital de Clinicas Niterói e Mário Lioni, Rio de Janeiro, Brazil*
*Critical Care* 2005, **9(Suppl 1):**P9 (DOI 10.1186/cc3072)

**Introduction** Ventilator-associated pneumonia (VAP) is very important in ventilated patients. There are many procedures (more or less 23) that could reduce VAP, but many of them are difficult or expensive to use

**Objectives** To evaluate the efficacy of three simple measures, the semi-recumbent position, 'clean' intubation and a protocol of tracheal aspiration, in the incidence of VAP

**Methods** Our ICU has 12 adult beds. The period was the year 2003 and 2004 until October. We standardized the semi-recumbent position at 45°, routine intubation and tracheal aspiration in all patients under mechanical ventilation. Nothing more changed. We compared the incidence of VAP in 2003 with the data from 2001, 2002 and 2004.

**Results** Patients were similar by age, sex and APACHE II score. The incidence of VAP was 28 and 22 per 1000 patient-days of mechanical ventilation in 2001 and 2002. The incidence in 2003 was 10.7, almost 50% less than 2001/2002, and 7.4 in 2004. In a study we had done in 2002, we identified in 80% of opportunities that patients under mechanical ventilation were with the trunk below 45°.

**Conclusion** To keep the patient under mechanical ventilation in a semi-recumbent position is not difficult, as to standardize intubation and tracheal aspiration. Unfortunately our doctors, nurses and respiratory therapists were not aware of these practices, although all of them know the rationale and advantages. With these simple and inexpensive measures, we could reduce significantly the incidence of VAP, around 50%. We must continue the study, with many cases, to confirm the results.

## P10

### Risk factor analysis of pneumonias developing after open heart surgery

**Y Bicer, S Simsek, N Yapici, O Aydin, F Sogut, Z Aykac**
*Siyami Ersek Thoracic and Cardiovascular Surgery Center, Istanbul, Turkey*
*Critical Care* 2005, **9(Suppl 1):**P10 (DOI 10.1186/cc3073)

**Introduction** Pneumonia after cardiac surgery have an important role among the infections that originate from hospitals as they increase mortality, morbidity and costs. To decrease the pneumonia incidence after open heart surgery, we should analyse the risk factors correctly and eliminate the preventable risk factors.

**Methods** In our study 1000 consecutive patients who had open heart surgery since January 2002 in Siyami Ersek Thoracic and Cardiovascular Surgery Center were followed about pneumonia prospectively. Pneumonia is defined with Center of Disease Control–ABD criteria. In identifications of microorganisms, classical methods and BBL Chrystal Gram Positive ve BBL Gram Negative (Becton Dickenson) kits were used. Data have been analysed statistically in the SPSS for Windows 10.0 programme. In univariant analysis a *t* test was used, in group variants chi square tests were used. $P < 0.05$ was considered statistically significant.

To determine the independent risk factors multivariant logistic regression analysis was used.

**Results** In 991 patients, data were found suitable for the study. The mean patients' age is 57.6 ± 13 years. Demographic data of the patients are shown in Table 1. The pneumonia ratio is 1000 device day/12.5. By univariant analysis age, emergency operation, low EF, operation time, intubation time, respiratory interventions, reintubation, enteral feeding, reoperation, resuscitation, presence of any complication, readmission to the ICU, and usage of blood derivatives are found to be the risk factors for pneumonia after cardiac surgery. Independent risk factors of pneumonia development are shown in Table 2.

**Table 1**

| | Percent |
|---|---|
| Female/male | 28/72 |
| Emergency | 6.4 |
| DM | 17 |
| EF < 40% | 4 |
| CABG | 67.5 |
| Valve replacement | 20 |
| Combine procedures | 3.3 |
| Other | 8.2 |

**Table 2**

| | *P* value | Odds ratio (95% CI) |
|---|---|---|
| Age > 68 years | 0.028 | 1.06 (1.0–1.12) |
| Emergency operation | 0.017 | 4.9 (1.33–17.93) |
| Entubation time | 0.001 | 2.0 (1.1–3.17) |
| Respiratory intervention | 0.005 | 4.8 (1.33–22.31) |
| Reintubation | 0.0001 | 14.47 (3.46–60.41) |
| Blood usage | 0.015 | 1.4 (1.0–1.8) |
| Readmission to ICU | 0.005 | 3.2 (1.93–11.02) |

**Conclusion** Nosocomial pneumonia is one of the most significant infections among cardiac surgery patients in the postoperative period. In different studies the frequency of nosocomial pneumonia was found between 0.2% and 9.7% and the mortality rate between 23% and 51%. According to our study older age and emergency-operated patients are under higher risk of pneumonia after cardiac surgery. The risk factors like intubation time, enteral feeding, usage of blood and blood derivatives must be controlled in preoperative, intraoperative and postoperative periods.

## P11

## Perinatal risk factors for early onset neonatal infection

**V Elvedji-Gasparovic, B Peter, T Klepac-Pulanic**
*KBC Zagreb, Petrova Klinika, Zagreb, Croatia*
*Critical Care* 2005, **9(Suppl 1):**P11 (DOI 10.1186/cc3074)

**Introduction** Neonatal infection and perinatal mortality rate are a big challenge to neonatologists and obstetricians as well. Group B streptococcal (GBS) infection is the most common early onset (EO) neonatal infection with an incidence of 1–4 per 1000 live born in the developed world.

**Methods** We studied the newborn infection rate before and after American Academy of Pediatrics (AAP) Protocol implementation in Croatia. The protocol for beta haemolytic streptococcal B infection includes: intrapartum antibiotic prophilaxis with ampicillin and gentamycin in preterm labour at < 37 weeks of gestation, premature rupture of membranes at < 37 weeks of gestation, fever during labour, ruptures of membranes >18 hours before delivery and previous delivery of a sibling with invasive GBS disease.

**Results** Of 784 neonates admited to the NICU, between 1 January 2003. and 31 December 2003, 60 (14 per 1000 live born) developed definite, culture confirmed, early onset (< 48 hours) GBS infection and seven (two per 1000 live born) developed probable infection (clinical signs consistent with EOGBS in a baby under 48 hours old, colonised with group B streptococci).

**Discussion** Conatal infection increases the sensitivity of the foetal brain to hypoxia and has later neuro risk sequelae to the newborn child. Our data suggest that the incidence of GBS infection in our country was considerably higher than in all current studies. Reasons for that can be inadequate perinatal screen in some parts of the country and no established policy for intrapartum antibiotic treatment of women with antenatal risk factors. In our study more than 80% of women who delivered neonates with EOGBS disease had at least one of the risk factors. After the year 2000, when we started the AAP Protocol, the incidence of infection decreased to 5/1000 live born infants. The mortality from EOGBS dropped to 3%.

**Conclusion** It is very important to establish a basis for trials of different strategies to reduce EOGBS infections in countries in transition with low social and economy status. Our results documented that the AAP Protocol for beta haemolytic streptococcal B infection can significantly reduce perinatal mortality of neonatal infection and sepsis.

## P12

## Urinary catheter-related infection in critically ill patients

**L Lorente, C Henry, M Martín, M Mora**
*Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain*
*Critical Care* 2005, **9(Suppl 1):**P12 (DOI 10.1186/cc3075)

**Objective** To determine the incidence and microorganisms responsible for urinary catheter-related infection (UCRI) in critically ill patients.

**Methods** It is a prospective study performed during 30 months of the patients admitted to a 24-bed medical–surgical ICU of a 650-bed university hospital. Urinary cultures were taken on admission and twice weekly. UCRI were diagnosed according to CDC criteria. UCRI were classified based on the onset moment as early onset and late onset: early onset were those developed during the first 4 days of the ICU stay; and late onset were those developed 5 days after ICU admission. The statistical analysis was performed using the SPSS 11.0 program. Continuous variables are reported as means and standard deviation, and categoric variables as percentages.

**Results** A total of 1582 patients were admitted, 953 males (60.24%). The mean age was 57.91 ± 18.83 years (median 63 years, interquartile range 44–73 years). The mean APACHE II score was 13.95 ± 8.93 (median 14, interquartile range 10–19). Admission diagnoses were: 737 (46.59%) heart surgery, 189 cardiological (11.95%), 196 neurologic (12.29%), 185 trauma (11.69%), 120 respiratory (7.59%), 104 digestive (6.57%) and 51 intoxication (3.22%). Mortality rate was 14.79% (234 patients). A total of 1392 patients (87.99%) needed a urinary catheter, during 12,556 days. Of the 1392 patients, 72 (5.17%) developed 75 UCRI (late onset in 54 cases and early onset in 21 cases). All UCRI were caused by only a microorganism. The incidence density was 5.97 UCRI/1000 urinary catheter-days. The microorganisms responsible for UCRI were the following: *Escherichia coli* (16), *Pseudomonas aeruginosa* (seven), *Morganella morganii* (four), *Klebsiella* (four),

*Citrobacter* (five), *Proteus mirabilis* (three), *Enterococcus faecalis* (eight), coagulase-negative staphylococci (seven), MSSA (two), *Candida albicans* (12) and other fungi (seven).
**Conclusions** In our series, most UCRI had a late onset, were caused by only a microorganism and were mainly due to *E. coli* and *C. albicans*.

## P13

### Serial changes in ICU-acquired pneumonia pathogen after the remodeling of the environment in a MICU

**S Hong[1], J Jung[1], C Lim[1], S Na[1], J Ahn[2], S Lee[1], W Kim[1], D Kim[1], Y Koh[1]**
*[1]Asian Medical Center, University of Ulsan College of Medicine, Seoul, South Korea; [2]Ulsan University Hospital, Ulsan, South Korea*
*Critical Care* 2005, **9(Suppl 1):**P13 (DOI 10.1186/cc3076)

**Introduction** The aim of the study was to observe effects of the improvement of the patient's care facility in a medical ICU (MICU) on ICU-acquired pneumonia (IAP), especially caused by drug-resistant bacteria including methicillin-resistant *Staphylococcus aureus*, third-generation cephalosporin-resistant *Acinetobacter baumanii* (ISAB), imipenem-intermediate sensitive *A. baumanii* (IIAB), imipenem-resistant *A. baumanii* (IRAB), expanded-spectrum beta-lactamase (ESBL), and imipenem-resistant *Pseudomonas aeruginosa* (IRPA).
**Methods** All critically ill patients with clinically diagnosed IAP between January 2001 and June 2002 (period 1 – before remodeling), October 2002 and March 2003 (period 2 – after remodeling) and October 2003 and March 2004 (period 3 – 1-year follow-up after remodeling) were observed prospectively in the 28-bed MICU of a 2100-bed tertiary-care singer center. Clinical suspicion of IAP was defined by a new and persistent infiltrate on chest radiography associated with at least two of the following: purulent secretions, temperature $\geq$ 38.5°C or $<$ 36.5°C, and a leukocyte count higher than 10,000/μl or lower than 4000/μl.
**Results** A total 1038 patients (355, 353 and 330) were admitted to the MICU during the study periods. At each period, 48 (44 cases, 11%), 38 (34 cases, 8%), and 80 (60 cases, 18%) episodes of clinically diagnosed IAP occurred ($P = 0.160$). The mean age (62 vs 66 vs 63, $P = 0.272$), percentage of males (82 vs 82 vs 78, $P = 0.800$), and mean APACHE III score (67.3 ± 18.7 vs 70.1 ± 26.5 vs 77.7 ± 28.0, $P = 0.148$) were not different during the study periods. Episodes of MRSA [13(30%) vs 12 (34%) vs 29 (37%)], ISAB [6 (13%) vs 1 (3%) vs 9 (11%), $P = 0.243$], IRPA [2 (4%) vs 1 (3%) vs 9 (11%), $P = 0.150$], and ESBL [2 (4%) vs 5 (13%) vs 4 (5%), $P = 0.180$] were not different during the study periods. Episodes of IIAB [4 (8%) vs 0 (0%) vs 0 (0%), $P = 0.006$] and IRAB [5 (10%) vs 0 (0%) vs 1 (1%), $P = 0.011$] were lower in periods 2 and 3 than in period 1. Duration of mechanical ventilation (22.2 ± 13.1 days vs 24.1 ± 13.0 days vs 20.0 ± 13.1 days, $P = 0.340$), and mortality in the ICU (54.5% vs 44.1% vs 38.3%, $P = 0.258$) were not different during the study periods. Use of carbapenem [9 (19%) vs 5 (13%) vs 29 (36%), $P = 0.011$] and glycopeptide [13 (27%) vs 10 (26%) vs 45 (56%), $P = 0.001$] were higher in period 3 than in periods 1 and 2, and third-generation cephalosporin [21 (44%) vs 20 (53%) vs 19 (24%), $P = 0.004$] was lower in period 3 than periods 1 and 2.
**Conclusion** The incidence of IAP caused by drug resistant bacteria was not affected by the improvement of the patient's care environment in the studied ICU. However, the incidence of IAP by IRAB and IIAB has been decreased after the remodeling.

## P14

### Duration of infusions and blood stream infections in polytrauma patients

**Y Nalapko, N Kachur, D Dokashenko**
*State Medical University, Lugansk, Ukraine*
*Critical Care* 2005, **9(Suppl 1):**P14 (DOI 10.1186/cc3077)

**Introduction** Central venous catheters (CVCs) are generally used in ICU patients. Nevertheless, bloodstream infections are common and dangerous complications of CVCs. The use of CVCs in ICU patients has contributed to the majority of nosocomial bloodstream infections caused by *Staphylococcus aureus*, *Staphylococcus epidermidis* and *Candida* species. It was shown that more than 200,000 cases of CVC-related bloodstream infections occur annually in the United States, with mortality of 12–25%.
**Objective** To evaluate the predictive value of the working time of a central venous line as a risk factor of blood stream infections in polytrauma patients.
**Materials and methods** In the period of 1 February 2002 to 30 November 2004, 451 patients with severe polytrauma were admitted to the ICU of Lugansk District Hospital. All of them had CVCs, and the average duration of stay in the ICU was 7.12 days (6–21 days). The working time of the CVC (WT CVC) and incidence of nosocomial blood stream infections were analyzed. Patients who died on the first to third day of hospitalization were excluded from the investigation as inappropriate to nosocomial infection criteria.
**Results** WT CVC was measured as the duration of infusions/transfusions during the first 7 days of the post-traumatic period. The incidence of blood stream infections was 21 cases (4.66%). All patients were divided into two groups: Group A, with blood stream infections (21 patients); Group B, patients who have no such complications (430 cases).
WT CVC in Group A and in Group B was 128.1 ± 11.5 hours and 87.5 ± 7.4 hours, respectively ($P < 0.05$).
Infusions of crystalloids, colloids, blood components and other medications prolonged round-a-day and depended on severity of injury, blood loss volume, and presence of multiple organ dysfunction. Severity of injury measured by the Trauma Score was 8.5 ± 1.1 and 9.7 ± 1.0, respectively ($P > 0.05$). Blood loss was 2.2 ± 0.6 l and 1.3 ± 0.2 l ($P < 0.05$), parameters of acute physiology (by SAPS) were 12.8 ± 0.8 and 9.4 ± 1.0, respectively ($P < 0.05$).
**Conclusion** Thus, incidence of blood stream infections depends on the duration of infusions/transfusions in the ICU. The WT CVC is defined by statistically considered factors – blood loss volume and severity of MODS. Severity of trauma is not a predictor of CVC blood infections.

## P15

### Five years of nosocomial Gram-negative bacteremia in a general systems intensive care unit

**W Sligl, G Taylor, P Brindley**
*University of Alberta, Edmonton, AB, Canada*
*Critical Care* 2005, **9(Suppl 1):**P15 (DOI 10.1186/cc3078)

**Objectives** Nosocomial Gram-negative bacteremia in the critically ill is associated with significant morbidity and mortality. This study provides epidemiological and antimicrobial susceptibility data for nosocomial Gram-negative bacteremia in a general systems ICU over a 5-year period.
**Methods** Positive blood cultures from 1 January 1999 to 31 December 2003 were reviewed for microbial etiology and susceptibilities. Patient charts were reviewed to determine the

source of infection, time from admission to bacteremia, causative organisms, antimicrobial susceptibilities, choice of empiric antibiotic therapy and outcome.
**Results** There were 1632 admissions with 45 nosocomial Gram-negative bacteremias in 44 patients. Infection rates of 28.2/1000 admissions and 12.1/10 000 patient-days remained stable over 5 years. The mean patient age was 55.3 years (range 17–86 years); 27.3% of patients were female, and 72.8% were male. The majority (95.6%) of bloodstream infections were monomicrobial, with only one episode of polymicrobial bacteremia. Common admitting diagnoses included respiratory failure, solid organ transplant, post-surgery, and multi-trauma. Seven bacterial species were identified; *Pseudomonas aeruginosa* and *Enterobacter* spp. were most common. Sources of bacteremia included pneumonia (48.9%), followed by central venous catheterization (22.2%). The mean time from admission to hospital to development of bacteremia was 32.9 days (95% confidence interval [CI] 0–100.9), and time from admission to the ICU was slightly less at 26.0 days (95% CI 0–90.1). Antimicrobial susceptibilities were highest for imipenem, gentamicin, tobramycin, ceftazidime, and piperacillin/tazobactam. Ciprofloxacin susceptibility was inferior to imipenem, gentamicin, and tobramycin ($P < 0.05$). Empiric coverage with an agent to which the microorganism was ultimately susceptible was 89.2%. The mortality rate was 53.3% in the ICU, and 60.0% for overall hospitalization, compared with an overall mortality rate of 11.7% for the year 2004 in our ICU patients. The average length of the ICU stay was 50.5 (95% CI 0–150.1) days compared with 6.13 (95% CI 4.29–7.97) days for all-comers.
**Conclusions** Nosocomial Gram-negative bacteremia is associated with marked morbidity and mortality in critically ill patients. Significant resistance to ciprofloxacin was demonstrated. Empiric treatment regimens should be based on unit-specific data.

## P16

### Epidemiology and etiology of nosocomial infections in a surgical intensive care unit

**B Gelfand, T Popov, V Karabak, B Belocerkovsky**
*Department of Surgery, Anaesthesiology and Intensive Care, State Medical University of Russia, Moscow, Russia*
*Critical Care* 2005, **9(Suppl 1):**P16 (DOI 10.1186/cc3079)

**Objectives** To assess the epidemiology and etiology of nosocomial infections (NI) and to identify patterns of antibiotic resistance in a surgical ICU.
**Setting** The ICU of 1st Clinic Hospital, Clinic of Surgery, Moscow.
**Methods** From September 2002 to December 2004 we conducted a prospective study and detected the most frequent NI in patients admitted for more than 48 hours to the ICU. The diagnosis of NI was defined according to CDC criteria. We also evaluated antimicrobial resistance of isolated microorganisms. The identification and susceptibility to antibiotics has been performed in automated system MIC/ID panels as described by the NCCLS.
**Results** During the study 2083 patients were admitted to the ICU, 1379 patients stayed more than 48 hours in the ICU. A total of 242 infection episodes were diagnosed in 149 patients with nosocomial infection (7.2%), 84 (56.4%) had a single infection, 48 (32.2%) had two infections, and 17 (11.4%) had three or more infections. Pneumonia were the most frequently reported type of infection (119 episodes, 49.1% of all cases of infection), followed by intra-abdominal infections (68 episodes, 28.1%), wound infections (28 episodes, 11.6%), laboratory confirmed bloodstream infections (14 episodes, 5.8%), urinary tract infections (eight episodes, 3%). About 43.0% infections were associated with sepsis, 43.8% with severe sepsis and 4.5% with septic shock, and 8.7% were not classified. The mortality rate for the ICU-acquired infections after 6 weeks of follow-up was 45.6%. Age ≥ 65 years (odds ratio [OR]: 4.08; 95% confidence interval [CI]: 2.05–8.11; $P < 0.001$), APACHE II score > 20 (OR: 10.70; 95% CI: 4.74–24.50; $P < 0.001$), SOFA > 5(OR: 15.6; 95% CI: 6.50–37.86; $P < 0.001$) were independently associated with mortality. The 246 isolated pathogens were represented by 92 Gram-positive cocci, 154 Gram-negative bacilli and 2% *Candida* species. *Staphylococcus aureus* (20.3%) was the most frequently isolated bacteria, followed by *Acinetobacter* spp. (18.3%), *Pseudomonas aeruginosa* (14.6%), *Klebsiella* spp. (13.4%), *Enterococcus* spp. (13.2%), *Escherichia coli* (8.1%). Resistance to oxacillin was observed for 94% of *S. aureus* isolates, all isolates were susceptible to vancomycin. The most active antimicrobial agents: against *Acinetobacter* spp. were imipenem (91.1%), ampicillin/sulbactam (64.4%); against *P. aeruginosa* were imipenem (88.9%), ceftazidime (69.4%), amikacin (58.3%); against *Klebsiella* spp. were imipenem (97%), amikacin (91%); against *E. coli* were imipenem (90%), amikacin (95%), ciprofloxacin (50%).
**Conclusions** The NI rate during the period was 7.2%. The mortality of the patients with a NI is 45.6%. Pneumonia were the predominant type of infection. Staphylococci were the most frequently isolated pathogens, with very high levels of MR.

## P17

### ICU stay promotes enrichment and dissemination of multi-resistant coagulase-negative staphylococcal clones

**C Agvald-Ohman, C Edlund, B Lund, J Struwe, G Hedin, H Hjelmqvist**
*Karolinska Institute, Huddinge, Sweden*
*Critical Care* 2005, **9(Suppl 1):**P17 (DOI 10.1186/cc3080)

**Introduction** Patients in the ICU are prone to be colonized and infected by multi-resistant bacteria [1,2]. It is previously known that nosocomial infections are often preceded by cross-transmission events [3].
The aim of the present investigation was to study the impact of the patient's length of ICU stay on the resistance patterns, clonal diversity and dissemination of coagulase-negative staphylococci (CoNS) within and between patients.
**Methods** Two groups of patients were studied, including 20 consecutive patients sampled within 2 hours from admission (shortstayers, SS), and all patients treated for at least 5 days at the ICU (longstayers, LS), available for sampling every second week ($n = 23$). Sampling was performed from five sites: oropharynx, nares, neck, axilla and perineum. A total of 868 CoNS isolates deriving from LS patients and 403 isolates from SS patients were analyzed for antimicrobial susceptibility, clonal diversity and dissemination within and between patients. All 1271 CoNS isolates were tested for antimicrobial susceptibility and subtyped to the clonal level according to their phenotype with the PhenePlate™ (PhP) system using PhP-CS plates (PhPlate Microplate Techniques AB, Stockholm, Sweden) designed for typing CoNS. The clonal relationship between CoNS isolates clustered as one phenotype isolated from at least two patients was further confirmed by pulsed-field gel electrophoresis.
**Results** The highest resistance rates were seen for oxacillin and ciprofloxacin, being 92% and 83%, respectively. LS were at significantly higher risk of being colonized with CoNS isolates resistant against oxacillin, clindamycin, ciprofloxacin, gentamicin as well as with multi-resistant strains. Genotyping revealed 16 clones that colonized more than one patient. One of the clones was isolated from 10 individuals, including two SS patients, indicating an epidemic strain.

**Conclusion** Prolonged ICU stay was significantly correlated to decreased clonal diversity, increased endogenous dissemination of resistant strains and cross-transmission. The results emphasize the importance of barrier treatment and other hygienic measures, especially in this vulnerable group of patients.

**References**

1. Maki DCC: **Line sepsis in the ICU: prevention, diagnosis and management.** *Seminar Resp Crit Care Med* 2003, **24:**23-36.
2. von Eiff C, Peters G, Heilmann C: **Pathogenesis of infections due to coagulase-negative staphylococci.** *Lancet Infect Dis* 2002, **2:**677-685.
3. Weist K, Pollege K, Schulz I, Ruden H, Gastmeier P: **How many nosocomial infections are associated with cross-transmission? A prospective cohort study in a surgical intensive care unit.** *Infect Contr Hosp Epidemiol* 2002, **23:**127-132.

## P18

### Evaluation of outcome in critically ill patients with *Acinetobacter baumannii* bacteremia

**M Pratikaki, C Routsi, E Platsouka, C Sotiropoulou, S Nanas, P Kaltsas, O Paniara, C Roussos**
*Evangelismos Hospital, Athens, Greece*
*Critical Care* 2005, **9(Suppl 1):**P18 (DOI 10.1186/cc3081)

**Objective** Bacteremia caused by *Acinetobacter baumannii* has an increasing incidence among critically ill patients. However, it is not clear whether it is associated with a higher mortality since controversial results have been reported. Increased mortality rate has been shown in some studies [1], whereas in others *A. baumannii* bacteremia does not alter the outcome [2]. The aim of this study was to evaluate the clinical impact of *A. baumannii* bacteremia on the outcome of patients in our ICU.

**Patients and methods** During a 4-month period (August–December 2004), in a 30-bed multidisciplinary ICU, patients who developed *A. baumannii* bacteremia and control patients without microbiological evidence of bacteremia were prospectively studied. Matching of control patients (1:2 ratio) was made on the basis of the APACHE II score (± 2 points) and diagnostic category.

**Results** During the study period, *A. baumannii* bacteremia was diagnosed in 21 patients (59 ± 15 years, mean ± standard deviation), admitted to the ICU (incidence 9.3 per 100 admissions). The APACHE II score in case and control patients was 19.9 ± 4.5 and 19.6 ± 4.8, respectively. The median interval from admission to the *A. baumannii* bacteremia was 10.5 days. *A. baumanii* strains were resistant to all antibiotics but susceptible to imipenem/cilastin and colistin. The ICU length of stay was 37 (23–51) days and 9 (1.8–16.2) days, median (95% confidence interval), for case and control patients, respectively, $P < 0.001$. Case patients had a longer duration of mechanical ventilation versus control: 21 (9–53) days versus 5 (2–18) days, respectively, $P < 0.001$. No differences between case and control patients were found in gender and age. Patients with *A. baumannii* bacteremia had significantly higher mortality than controls (38.1% vs 7.15%, $P = 0.004$). Logistic regression analysis showed that risk factors that were independently associated with adverse outcome were the presence of bacteremia (odds ratio = 10.2, $P = 0.013$), and multisystem organ failure (odds ratio = 20.9, $P = 0.001$).

**Conclusions** In this group of critically ill patients, after adjustment for severity of acute illness, *A. baumannii* bacteremia was associated with a significantly increased mortality rate compared with matched control patients. Whether other factors contribute to this increase has to be examined.

**References**

1. *Crit Care Med* 1999, **27:**1794-1799.
2. *Intensive Care Med* 2003, **29:**471-475.

## P19

### Evolution of resistance in *Acinetobacter baumannii* in a Tunisian intensive care unit after antibiotherapy restriction

**N Brahmi, Y Blel, N Kouraichi, A Mokline, N Laabidi, O Beji, H Thabet, M Amamou**
*CAMU, Tunis, Tunisia*
*Critical Care* 2005, **9(Suppl 1):**P19 (DOI 10.1186/cc3082)

**Introduction** The prevalence of carbapenem-resistant isolates of *Acinetobacter baumannii* is increasing in Tunisian ICUs. The wide use of antibiotherapy is implicated certainly in this mechanism of resistance.

**Objective** The purpose of this study is to evaluate the evolution of *A. baumannii* resistance after a new strategy of prescription consisting of controlling and restriction of antibiotherapy prescription.

**Materials and methods** Evolution of resistance of all *A. baumannii* isolates is compared between 2001 (before antibiotherapy restriction) and 2003–2004 (after).

**Results** See Table 1.

**Table 1**

| % of resistance | 2001 ($n = 134$) | 2003 ($n = 50$) | $P$ | 2004 ($n = 63$) | $P'$ |
|---|---|---|---|---|---|
| Ticarcilline | 76 | 63 | 0.05* | 77 | 0.8 |
| Piperacilline | 97 | 85 | 0.01* | 81 | $10^{-3}$* |
| Ceftazidim | 95 | 84 | 0.01* | 79 | $8 \times 10^{-4}$* |
| Carbapenem | 37 | 37 | 0.36 | 25 | 0.09 |
| Amikacine | 85 | 70 | 0.28 | 68 | $6 \times 10^{-3}$* |
| Netilmycine | 30 | 31 | 0.86 | 31 | 0.7 |
| Ofloxacine | 95 | 87 | 0.04* | 93 | 0.9 |
| Ciprofloxacine | 95 | 87 | 0.16 | 94 | 0.9 |

$P$, 2003 – 2001; $P'$, 2004 – 2001. * $P < 0.05$.

**Conclusion** With antibiotherapy restriction we have obtained a significant reduction of resistance for piperacillin, ceftazidim and amikacin. We have obtained also a decrease of carbapenem-resistant isolates (37% vs 25%) but not significant enough if compared with other countries (5% in New York and 11% in Brazil).

## P20

### Epidemiological profile and antibiotic susceptibility of *Pseudomonas areuginosa* isolates within the hospitalized burned patient

**K Bousselmi[1], L Thabet[2], S Oueslati[1], O Ben Jaber[1], A Ouchtati[1], S Cherif[1], S Ben Redjeb[2], A Messadi[1]**
*[1]Aziza Othmana Hospital, Tunis, Tunisia; [2]Faculty of Medicine of Tunis, Tunisia*
*Critical Care* 2005, **9(Suppl 1):**P20 (DOI 10.1186/cc3083)

*Pseudomonas aeruginosa* plays a predominant role as an etiological agent involved in serious infections in burned patients. Treatment of these infections is frequently complicated by antibiotic resistance, a problem that has been increasing in recent years.

The objective of this study is to analyse the epidemiological profile and antibiotic susceptibility of *P. aeruginosa* isolates within the burned patients admitted to our intensive care burn department.

During a period of 4 years (2000–2003), 828 burn patients were admitted. Thermal burn (70%) was the most frequent burn,

followed by electric (27%) and chemical (3%) burn. The population examined had an average burn size of 44% of the body surface with the mean age of 34 ± 17 years. One hundred and seventy strains of *P. aeruginosa* were isolated in different samples from burned patients. These isolates were identified using standard microbiological techniques and their antibiotic susceptibility was determined using the disk diffusion method recommended by the French Society of Microbiology.

Over the study period, *P. aeruginosa* was isolated mainly from cutaneous superinfections (59%), urine (21.7%), blood culture (14.8%) and venous catheter culture (4.7%). *P. aeruginosa* was the most common isolate from cutaneous pus (22.9%). Bacteremia were mainly caused by *Acinetobacter baumannii* (16.5%) and *Staphylococcus aureus* (15.5%). *P. aeruginosa* was only isolated in 8.2% of bacteremia. The survey of antibiotic susceptibility of *P. aeruginosa* showed that 60.9% of strains were resistant to piperacillin, 53.4% to ceftazidime, 37.6% to imipenem, 70.6% to cefsulodine, 59.3% to tobramycin, 80% to gentamicin, 62.4% to amikacin and 53.4% to ciprofloxacin.

During this study period, a high resistance to antibiotics of *P. aeruginosa* was observed. It is necessary to implement urgent measures to prevent the spreading of these multi-resistant strains. These measures include: sensible limitation of the use of antimicrobial agent, strict disinfection and hygienic procedures.

## P21

### Strategy of antimicrobal therapy in patients with severe trauma: importance of initial severity state evaluation

**A Yaroshetskiy[1], D Protsenko[2], S Yakovlev[3], B Gelfand[2]**
*[1]City Hospital #7, ICU, Moscow, Russia; [2]State Medical University of Russia, Moscow, Russia; [3]Moscow Medical Academy, Moscow, Russia*
*Critical Care* 2005, **9(Suppl 1):**P21 (DOI 10.1186/cc3084)

**Introduction** A high rate of nosocomial infections among patients with severe multiple trauma including severe traumatic brain injury and initial APACHE II score of 15 or more leads to increased length of stay (LOS), costs and high mortality. That makes the prevention of severe nosocomial infections one of the major therapeutic interventions in these patients. Because of a high rate of mixed nosocomial infections with high resistance to antibiotics it is necessary to start antimicrobal therapy with extended-spectrum antibiotics. Taking into account pharmacodynamics, pharmacokinetics and microbiological features of carbapenems, they make the best choice for these patients. In the case of MRSA infection it is necessary to use the combination of carbapenem and vancomycin.

**Objective** The goal of the study was to assess the influence of maximal initial antimicrobal therapy with meropenem on mortality, rate of nosocomial infections and LOS in the ICU in patients with severe trauma including severe traumatic brain injury and initial APACHE II score of 15 or more.

**Results** The study was performed in a general ICU from April 2003 to September 2004. All patients with severe trauma with predominant severe traumatic brain injury and initial APACHE II score of 15 or more were included in the study. We studied two groups of patients. In the case of known or suspected nosocomial infection, patients in the maximal antimicrobal therapy (MAT) group ($n = 16$, APACHE II 19.88 ± 3.6) received meropenem 3–6 g/day depending on body weight for 14 days. In the case of proven MRSA infection, vancomycin 2 g/day was added. Patients in the control group ($n = 22$, APACHE II 19.90 ± 3.7) with known or suspected infection received initial antimicrobal therapy with cefalosporines 3 or fluoroquinolones with change of antimicrobal therapy according to microbiological data. The observed data did not follow the normal distribution. Comparisons between groups were performed using the chi-square test. Mortality in the MAT group was 6.25% (1/16), and in the control group was 50% (11/22), $P = 0.002$. Nosocomial infection rate (ventilator-associated pneumonia, meningitis) was observed in 31.25% of patients (5/16) in the MAT group and in 91% of patients (20/22) in the control group, $P < 0.001$. LOS in the ICU did not differ between groups (19.44 ± 3.1 in the MAT group and 18.09 ± 10.3 in the control group). But comparision between LOS among survivors in the two groups revealed significant reduction in LOS in the ICU in the MAT group (19.42 ± 3.2 in the MAT group and 25.54 ± 11.1 in the control group, $P < 0.05$).

**Conclusions** Initial antibiotic therapy with meropenem in patients with severe trauma including severe traumatic brain injury and initial APACHE-II score of 15 or more leads to a reduction in mortality, nosocomial infection rate and LOS in the ICU.

## P22

### Surveillance of ICU-acquired infections: intensive care unit characteristics, practices in prevention and surveillance methodology

**I Morales, C Suetens, A Versporten, C De Laet, K Mertens**
*Scientific Institute of Public Health, Brussels, Belgium*
*Critical Care* 2005, **9(Suppl 1):**P22 (DOI 10.1186/cc3085)

**Introduction** The characteristics and practices of ICUs participating in the Belgian national surveillance program were reviewed within the validation study. The main objective was to better understand the hospital practices for nosocomial infection prevention and the methodology used for the collection of surveillance data.

**Methods** Forty-five ICUs were randomly selected through systematic random sampling from a list of 1997–2001 participation-quarters (3 months). The number of patients admitted to the hospital and to the ICU was provided by the hospital administration as well as the number of hospitalization-days. Data were collected, through a questionnaire, from those responsible for data collection at each institution.

**Results** Data from 44 ICUs were analyzed. The average participation was six surveillance quarters (range 1–22). The ICUs belong to hospitals admitting on average 2676 patients per quarter. The average ICUs have 10.5 beds on average, and 88.6% of them are medical/surgical ICUs. The average number of ICU admissions was 217 patients per quarter (927 patient-days). The mean length of stay within the ICU was 4.3 days. Specific guidelines for pneumonia prevention were available in 75% of ICUs; and for catheter-related bacteremia in 85.4%. A total 86.4% of ICUs had specific guidelines for hemoculture procedures. Systematic culture of sputum (surveillance cultures) was performed by 77.3% ICUs, but with different periodicity. Catheter tip culture was performed by 73.8% of the ICUs (2/3 systematically). Guidelines for the use of antibiotics were available at 64% of ICUs while 15.8% of them allowed antibiotic use at the doctor's appreciation. Almost 70% of respondents prefer a patient-based rather than a unit-based surveillance. On average two persons are involved in surveillance (44% ICU doctor, 26% ICU nurse, 6% infection control doctor and 18% IC nurse). It takes 20 min per patient.

**Conclusions** The study allowed identifying methodological problems and areas for targeted training in order to improve the quality of the data collected in the national surveillance.

## P23

### Monitoring of the antibiotic prescriptions in order to prevent microbial resistance in the intensive care unit in the Russian hospital

**T Lugovkina[1], B Richards[2], F Badaev[1], A Piontek[1], V Bagin[1], V Shilova[3]**
*[1]Clinical Hospital N40, Yekaterinburg, Russia; [2]UMIST, Manchester, UK; [3]Center of Laboratory Diagnostics of Diseases of Mother and Child, Yekaterinburg, Russia*
*Critical Care* 2005, **9(Suppl 1):**P23 (DOI 10.1186/cc3086)

**Background** This presentation shows how, at the City Hospital, it was possible to improve the quality of clinical practice in surgery departments and ICUs.
**Introduction** Antibiotics play an important role in clinical practice. The expenditure on these drugs is more than 50% of the total expenditure for drugs at the hospital. Uncontrolled use of antibiotics, in the environment of intolerably poor financing of the hospitals in Russia, and the absence of adequate control of the antibiotic prescriptions induce the growth of resistance in the hospital microbial flora, and as a result the expenditure on drug treatment increases.
**Methodology** An analysis of the antibiotics purchased by the administration of the hospital was made in order to determine the baseline proportions of the different classes of antibiotics in the total structure in the year 2003. The analysis showed a high percentage of beta-lactams in the structure of the antibiotics purchased (88%).
The data from the Diagnostic Laboratory Center of the city were impressive: the level of *Klebsiella pneumoniae* producing the enlarged-spectrum beta-lactamases reached a level of 92.5% in the ICU. An analysis of patients' data at the ICU and surgical departments (in a cohort of 300) was made in order to evaluate the quality and appropriateness of the antibiotic prescriptions. An inappropriate choice of antibiotics, wrong dosage, or an incorrect timing regime were revealed in 60% of cases. The protocols of antibiotic prophylaxis and the strict rules of antibiotic prescriptions in the ICU, prepared according to the data of evidence-based medicine, were implemented.
**Conclusion** The system of governance of antibiotic prescriptions, the monitoring of the microbial resistance in the ICU, and the strict adherence to the protocols of antibiotic usage have gained approval and enabled an improvement in the quality of treatment (from 60% to 30%) and a reduction of the expenditure for antibiotics (40%).

## P24

### De-escalation therapy: 1-year experience in a general intensive care unit

**E Gyurov, S Milanov, M Georgieva, M Milanov**
*University Hospital, Sofia, Bulgaria*
*Critical Care* 2005, **9(Suppl 1):**P24 (DOI 10.1186/cc3087)

**Introduction** First-line choice of antibiotic treatment is an important issue for successful outcome in surgical and trauma patients. De-escalation strategy aims to improve the first choice of antibiotic therapy, to improve outcome and to save money.
**Setting** A general ICU, 17 beds, annual admission approximately 800 patients.
**Objective** To compare rates of success and failure of the empiric treatment of patients with usually prescribed antibiotics and the use of carbapenems with subsequent de-escalation.
**Method** Taking data from flow-charts, we determined the most frequently prescribed empiric antibiotics in our ICU during 2002 and calculated the rates of success and failure of the treatment. We considered the failure an inadequate antibiotic therapy. As shown in Table 1, there were two regimens used in 2002. The use of mefoxin was quite disappointing with only a 30% success rate. When other empiric antibiotic, or combination of antibiotics were used the rate of success was slightly below 50%. This can be partly explained with the high rate of surgical complications. In 2003–2004 we accepted for use the de-escalation strategy. Starting empiric carbapenems (tienam in 106 patients, meronem in 31 patients), we obtained samples for the microbiological laboratory from the sites of suspected infection. After receiving positive results we de-escalated antibiotic therapy according to susceptibility. The rate of success increased 11%, and the cases of inadequate empiric therapy fell to 4.4% of cases. Mortality rate decreased from 31% to 13%.
**Conclusions** Introducing de-escalation strategy into our clinical practice showed promising results. The percentage of cases of treatment failure (inadequate empiric antibiotic therapy) and the mortality rate decreased significantly. We need a longer period to confirm these result, as well as to analyze cost-effectiveness.

**Table 1 (abstract P24)**

| Antibiotics | Patients | Success rate | Escalation rate | De-escalation | Failure | Surgical complication | Death |
|---|---|---|---|---|---|---|---|
| 2002, mefoxin | 85 | 26 (31%) | 41 (48%) | – | 24 (28%) | 17 (20%) | 31 (36.4%) |
| 2002, other antibiotic | 114 | 53 (46.5%) | 30 (26.3%) | – | 15 (13%) | 25 (22%) | 30 (26.3%) |
| 2003–2004, carbapenems | 137 | 78 (57%) | – | 33 (24%) | 6 (4.4%) | 10 (7.3%) | 18 (13%) |

## P25

### The importance of antibiotics in animal models of sepsis

**MO Maybauer[1], DM Maybauer[1], JF Fraser[2], LD Traber[1], K Murakami[1], A Mizutani[1], P Enkhbaatar[1], N Morita[1], M Westphal[1], DL Traber[1]**
*[1]University of Texas Medical Branch, Galveston, TX, USA; [2]University of Queensland, Brisbane, Australia*
*Critical Care* 2005, **9(Suppl 1):**P25 (DOI 10.1186/cc3088)

**Objective** Our group developed an ovine model of *Pseudomonas aeruginosa* sepsis associated with acute lung injury (ALI) [1]. The aim of this study was to modify this model by the administration of Ceftazidime (Cef) to simulate a more clinically relevant situation. In addition we studied the effects of recombinant human activated protein C (rhAPC), as well as an combined treatment of rhAPC and Cef. This modification could be the basis for future studies investigating new treatment strategies in sepsis.
**Methods** Thirty sheep (35–40 kg) were operatively prepared for chronic study. After 7 days of recovery, sheep were randomly allocated either to sham, control, Cef, rhAPC, or Cef + rhAPC groups ($n = 6$ each). After a tracheostomy, ALI was produced and *P. aeruginosa* were instilled into the lungs, following an established protocol [1]. The sham group received the vehicle. The sheep were studied for 24 hours in the awake state and were ventilated with 100% oxygen. The $PaO_2/FiO_2$ ratio was determined at baseline (BL) and every 3 hours. Ceftazidime (3 g) was administered intravenously 1 and 13 hours post injury. rhAPC was given as a continuous infusion (24 μg/kg/hour), starting 1 hour post injury.

The animals were resuscitated with Ringer's lactate solution to maintain filling pressures and hematocrit. Statistical analysis: two-way analysis of variance and Student–Newman–Keuls post hoc comparisons. Data are expressed as mean ± standard error of the mean. Significance $P < 0.05$.

**Results** The $PaO_2/FiO_2$ ratio remained stable in sham (BL: 518.3 ± 12.7 vs 12 hours: 507.3 ± 18.8) animals. The control group showed a significant decrease in $PaO_2/FiO_2$ ratio (BL: 496.8 ± 21 vs 12 hours: 83.5 ± 9.8). The Cef group also showed a fall in $PaO_2/FiO_2$ ratio (BL: 524 ± 11.4 vs 12 hours: 173 ± 47), as well as the rhAPC (541.3 ± 12.2 vs 12 hours: 150.7 ± 28.6) group. In both groups there was a significant improvement of the $PaO_2/FiO_2$ ratio compared with the control group. The $PaO_2/FiO_2$ ratio of the Cef + rhAPC group (525.4 ± 9.9 vs 12 hours: 335.8 ± 25.8) was significantly higher than all other injured groups.

**Conclusion** Since the application of Cef + rhAPC after ALI associated with bacterial challenge improved pulmonary function more than Cef or rhAPC alone, it underlines the importance of antibiotic treatments for further studies in animal models of sepsis.

**Acknowledgements** Grant support from Shrine 8820, 8450, NIH GM066312.

**Reference**

1. Murakami, *et al.*: *Crit Care Med* 2002, **30:**2083-2090.

## P26

### Outbreak of severe *Clostridium difficile*-associated colitis with MOF in Quebec intensive care units: first analysis in Sherbrooke ICUs

**F Lamontagne, M Lalancette, O Martinet, J Pepin, O Lesur**
*CHU Sherbrooke, Canada*
*Critical Care* 2005, **9(Suppl 1):**P26 (DOI 10.1186/cc3089)

**Introduction** Recent reports suggest that *Clostridium difficile* colitis (CDAC) may be evolving into a more severe disease [1]. Over the past 2 years, an increased case fatality associated with CDAC was noted as the admission rate to our adult tertiary ICUs for this entity increased in a context of inhospital outbreak. This CDAC outbreak occurred in a 682-bed regional hospital in Quebec, Canada. All cases admitted to ICUs with a diagnosis of life-threatening CDAC were systematically reviewed over a 20-month period (between 1 January 2003 and 21 August 2004). The following is a retrospective statistical analysis.

**Results** Until now, 41 cases of CDAC requiring intensive care monitoring and treatment have been collected; 53.7% were of male sex and the median age was 78 years (25th–75th %: 71–82). The Charlson morbidity index was calculated for each patient for a median of 4 (25th–75th %: 3–6). Patients were generally exhibiting a sepsis profile with high-grade fever (median 39.20°C, 25th–75th %: 38.7–39.4°C), and high leukocyte counts (median 28.15 × $10^9$/l, 25th–75th %: 20.8–43.7) at some time during the ICU stay. Serum creatinine levels were elevated (median 204 µmol/l, 25th–75th %: 139–292 µmol/l). Shock status was diagnosed in 83% of the patients and catecholamines were mandatory in 53.7% of the time for a mean duration of 3.4 days (± 0.47) in addition to volume resuscitation. Patients were resuscitated during the first 72 hours following their ICU admission with a mean of 10.7 $cm^3$ (± 986 $cm^3$) of crystalloid solution, 586 $cm^3$ Pentastarch solution (± 92 $cm^3$) and 231 $cm^3$ of 25% albumin (± 75 $cm^3$). Upon entry to the ICUs, the APACHE II score was calculated and the median obtained was of 24 (predicted mortality rate 49.7%). Furthermore, the SOFA score was also obtained upon entry, 48 hours after admission and every subsequent week. In the first 48 hours, the total SOFA score increased in 26.8% and decreased in 31.7% of the patients. Thirty-two percent of the population reached the maximum cardiovascular SOFA score of 4 (i.e. norepinephrine > 0.1 µg/kg/min). Twenty-two percent of patients went to the operating room.

The overall observed mortality rate was 49%. An APACHE II score upon entry of 22 or more and an age greater than 75 were both associated with higher mortality with an adjusted odds ratio (OR) of 7.6 (95% confidence interval [CI] 1.6–33.9, $P = 0.01$) and 4 (95% CI 1.06–15,1 $P = 0.07$). A trend toward higher mortality was observed in patients with an increasing SOFA score within the first 48 hours of admission (OR 4.55, 95% CI 0.91–22.6, $P = 0.1$) and high serum lactate levels (OR 18.8, 95% CI 0.97–362, $P = 0.03$ for lactates > 6.5) but no trends were noted regarding the Charlson comorbidity index, the decision of surgery (colectomy for bowel perforation vs refractory shock) or catecholaminergic drug use.

**Discussion** This case review reveals the existence of an outbreak of CDAC with increasing case fatality and worsening outcome in Quebec. Epidemiologic data will help in defining more efficient preventive measures directed toward this nosocomial entity and allowing early recognition in order to thwart severe illness.

**Reference**

1. Pepin J, *et al.*: *JAMC* 2004.

## P27

### Antimicrobial resistance in bloodstream infection does not affect outcome in intensive care unit patients with acute renal failure treated with renal replacement therapy

**E Hoste, S Blot, G Verschraegen, J De Schuijmer, S Claus, J De Waele, A Dhondt, R Vanholder, N Lameire, J Decruyenaere**
*Ghent University Hospital, Gent, Belgium*
*Critical Care* 2005, **9(Suppl 1):**P27 (DOI 10.1186/cc3090)

**Background** Bloodstream infections (BSI) have a worse outcome when the microorganisms involved are antimicrobial resistant (AM-R), compared with BSI with antimicrobial susceptible (AM-S) microorganisms. We evaluated whether this is also true in ICU patients with acute renal failure who are treated with renal replacement therapy (ARF-RRT), a particular severely ill cohort of ICU patients.

**Methods** All ARF-RRT patients with BSI admitted in our 54-bed tertiary care ICU during the period 1995–2002 were included in the study. Enteroccci were defined AM-R when resistant to vancomycin, staphylococci when resistant to methicillin, Gram-negative bacteria when resistant to ceftazidim, Pseudomonas when resistant to ceftazidim, quinolones, piperacilin, or imipenem, and Candida when resistant to fluconazole. Catheter-related BSI and BSI of unknown origin were defined as primary BSI. Data are presented as number (percentage) or median (interquartile range).

**Results** During the 8-year study period, 79 out of 1032 ARF-RRT patients (7.7%) developed BSI, incurring 88 different microorganisms. AM-R was present in 50 patients (63%). Gram-positive bacteria were more frequent in patients with AM-R BSI (72% vs 24%, $P < 0.001$), whereas Gram-negative bacteria (24% vs 53%, $P = 0.006$) or Candida (2% vs 18%, $P = 0.008$) were less frequent. A higher proportion of patients with AM-R BSI had primary BSI (58% vs 17%, $P < 0.001$). Patients with AM-R BSI and AM-S BSI had the same age (57 [42–67] years vs 62 [53–69] years, $P = 0.150$), and APACHE II score on admission (26 [17–32] vs 28 [18–37], $P = 0.338$). Time to BSI after start of RRT was longer in the AM-R group (11 [6–21] days vs 5 [1–19] days, $P = 0.026$). Patients with AM-R BSI had a higher need for vasopressor therapy (80% vs 52%, $P = 0.008$). Length of hospital stay was not different (42 [26–73] days vs 31 [16–75] days, $P = 0.528$) as was inhospital mortality (64% vs 72%, $P = 0.443$). Cox regression analysis identified, after adjustment for various covariates, older age (hazard ratio = 1.03 per year, 95% confidence interval:

1.01–1.05, $P = 0.02$), and primary BSI (hazard ratio = 0.42, 95% confidence interval: 0.21–0.85, $P = 0.02$) as associated with hospital mortality. There was no significant association between AM-R BSI and hospital mortality.
**Conclusions** In a subset of ICU patients with ARF-RRT, antimicrobial resistance of microorganisms that caused BSI did not affect mortality. After adjustment for various covariates, older age was associated with higher mortality. In addition, primary BSI was associated with lower inhospital mortality.

### P28

### Evaluation of adequacy in empirical antibiotic therapy in a general intensive care unit

**G Friedman, T Lisboa, R Moraes, E Parolo, L Mallmann**
*Hospital de Clinicas, Porto Alegre, Brazil*
*Critical Care* 2005, **9(Suppl 1):**P28 (DOI 10.1186/cc3091)

**Introduction** Infectious pathologies are among the most prevalent in the ICU and significantly influence the outcome of critically ill patients. However, the emergency of resistant pathogens to different antibiotics makes the choice of the initial treatment more complex. In addition, inadequate empirical antibiotic therapy is associated with a poorer outcome.
**Objectives** To evaluate the adequacy of antibiotic therapy in a general ICU and to collect data about the microbial flora in order to better adapt the empirical treatments.
**Materials and methods** Data were prospectively collected in a 12-bed general ICU. The presence of infection was defined by the doctor in charge of the patient. Inadequate antibiotic therapy was defined as microbiological evidence of infection not covered by the chosen antibiotics, or by the finding of primary resistance to the antibiotics in use.
**Results** Data were collected in 80 consecutive patients. The main site of infection was the lung (50%). The most prevalent microorganisms were the Gram-negative (52%). The prevalence of nosocomial infections was 60%. Empirical antibiotic therapy was inadequate in 28 episodes (35%), and the most prevalent microorganisms in this group were MRSA, Pseudomonas MR, *Stenotrophomonas maltophilia*. The general mortality rate was 40%, but the mortality rate among patients with inadequate antibiotic therapy was 50%, but only 33% when adequate antibiotic therapy (odds ratio = 3.09, 95% confidence interval 1.06–9.16). Risk factor to an inadequate therapy was nosocomial infection (relative risk 2.07, 95% confidence interval 1.01–4.26). Other risk factors that showed a non-significant trend were a delay to starting antibiotics greater than 24 hours, immunosupression, septic shock and higher APACHE II score. The number of empirical treatment schemes was 17.
**Conclusion** These preliminary data showed that there is an excess in mortality rate when empirical therapy is inadequate. The inadequacy of treatment was associated with nosocomial infections. There was an exaggerated variability on the choice of empirical strategy.

### P29

### Usefulness of quantitative analysis of beta-D-glucan in empirical therapy for systematic Candida infection in critically ill patients

**I Kano, T Kamohara, K Ikegami, H Taguchi, K Kawamura, J Yazawa, T Mouri**
*Dokkyo University School of Medicine, Koshigaya Hospital, Koshigaya, Japan*
*Critical Care* 2005, **9(Suppl 1):**P29 (DOI 10.1186/cc3092)

**Background** The clinical importance of systemic Candida infection in critically ill patients is a well-documented fact. However, it is not always true that early recognition of Candida infections followed by early pre-emptive antifungal therapy has been routinely done. Lack of an institutional written protocol for systemic Candida infections may lead to delayed diagnosis and treatment of such infections. It is expected that each institution has to establish its own clinical path to ensure a standardized team approach to systemic Candida infections to improve patient outcome.
**Purposes** One is to review indications of antifungal therapy and evaluate the relationship between risk factors and values of beta-D-glucan. Another is to test usefulness of risk factors to predict the increased value of beta-D-glucan prospectively.
**Patients and methods** Clinical records of 43 patients who received antifungal therapy for clinical diagnosis of systemic Candida infections were reviewed. Risk factors (APACHE score, Injury Severity Score [ISS], length of ICU stay, duration of mechanical ventilation, total blood transfusion within 48 hours, total parenteral nutrition, and signs of systematic inflammation), bacteriological studies, and quantitative data of beta-D-glucan (Fungitec G test MK, Seikagaku-kogyo, Japan) were analyzed. In a prospective study, 38 patients were followed to test the hypothesis that the risk factors (APACHE score >15 and ISS >16, ICU stay > 7 days, and mechanical ventilation > 2 days) can predict increased levels of beta-D-glucan (> 20 pg/ml), which validate pre-emptive antifungal therapy.
**Results** In a retrospective study, positive culture for Candida remained low (37.2%); however, beta-D-glucan was increased significantly (> 20 pg/ml) in 79.5% of patients. In patient with APACHE score >15 and ISS >16, beta-D-glucan was increased in 78.4%. Beta-D-glucan was also increased in 79.0% of patients who stayed in the ICU longer than 7 days. In prospective study, 26.3% (10/38) of patients eventually received antifungal agents. Of these, eight patients (80.0%) fulfilled APACHE score >15, ISS >16, and ICU stay > 7 days.
**Discussion** A certain combination of risk factors of systemic Candida infections was useful to identify the patient group who need pre-emptive antifungal therapy. Beta-D-glucan, which is a useful serologic test for fungal infections, was useful to initiate antifungal therapy in critically ill patients who fulfilled risk factors.
**Conclusions** APACHE score >15, ISS >16 and ICU stay > 7 days were useful to discriminate patients who are prone to develop systemic Candida infections. Beta-D-glucan (> 20 pg/ml) is a useful clinical tool to initiate pre-emptive antifungal therapy in such circumstances.

### P30

### Fungal colonization and infection in critically ill patients

**L Lorente, C García, M Martín, M Mora**
*Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain*
*Critical Care* 2005, **9(Suppl 1):**P30 (DOI 10.1186/cc3093)

**Objective** To determine the incidence of fungal colonization and infection in critically ill patients.
**Methods** It is a prospective study during 30 months of the patients admitted to the ICU during 24 hours or more. A throat swab, tracheal aspirate and urine samples were taken on admission and twice weekly. The fungal colonization and infection were registered. Infections were diagnosed according to CDC criteria. Infections were classified based on throat flora as: primary endogenous (PE) when caused by germs that were already colonizing the throat on ICU admission; secondary endogenous (SE) when caused by germs that were not colonizing the throat on the ICU admission but were acquired during the stay in ICU; exogenous (EX) when caused by germs that were not colonizing the throat. Infections were classified based on the onset moment as: early onset (EO) (developed during the first 4 days of ICU stay) and late onset (LO) (developed 5 days after ICU admission).

**Results** A total 1582 patients were admitted, 953 males (60.24%). Mean age was 57.91 ± 18.83 years. Mean APACHE II score was 13.95 ± 8.93. Admission diagnoses were: 737 (46.59%) heart surgery, 189 cardiological (11.95%), 196 neurologic (12.29%), 185 trauma (11.69%), 120 respiratory (7.59%), 104 digestive (6.57%) and 51 intoxication (3.22%). Mortality rate was 14.79% (234 patients). A total of 154 patients had fungal colonization, 40 patients at ICU admission and 114 patients during the ICU stay. Forty-eight fungal infections were documented (eight EO and 40 LO; four PE, 40 SE and four EX): 19 urinary tract infections (three EO and 16 LO; three PE, 13 SE and three EX), 12 pneumonias (two EO and 10 LO; one PE, 10 SE and one EX), nine primary fungemias (two EO and seven LO; nine SE), six surgical wounds (one EO and five LO; six SE) and two pressure sores (0 EO and two LO; two SE). The 48 fungi responsible for 48 fungal infections were: 29 *Candida albicans*, 12 *Candida tropicalis*, four *Candida glabrata*, two *Candida parapsilopsis*, one *Candida famata*. Death occurred in 12/48 patients (25%) with fungal infection: 3/9 (33.33%) fungemias, 5/12 (41.66%) pneumonias and 4/27 (14.81%) other infections.
**Conclusions** Most fungal infections had a late onset, were secondary endogenous and were due to *C. albicans*. The urinary tract was the more frequent origin.

## P31

## Leptospirosis in the intensive care unit: a cohort of 57 patients

**S Vieira[1], J Brauner[1], D Fonseca[2]**
*[1]Clinicas Hospital, Porto Alegre, Brazil; [2]NS Conceição Hospital, Porto Alegre, Brazil*
*Critical Care* 2005, **9(Suppl 1):**P31 (DOI 10.1186/cc3094)

**Introduction** Leptospirosis is in general a self-limited disease but it can be associated with important complications such as multiple organic dysfunction and high mortality [1,2].
**Objective** The goal of this paper is to evaluate the clinical characteristics and the morbimortality of severe leptospirosis in general ICUs from two general hospitals.
**Methods** All cases with the diagnosis of leptospirosis confirmed by a blood macroagglutination test and admitted from 1990 to 2004 were studied. We analyzed their clinical and laboratory characteristics, the occurrence of multiple organ dysfunction and their mortality rate. We also compared survivors with nonsurvivors. The quantitative variables have been compared by unpaired *t* test and the qualitative variables by a chi-squared test.
**Results** We describe 57 adult patients, 40 ± 16 years, 47 men and 10 women. The most frequent clinical manifestations were fever ($n = 52$), myalgias ($n = 51$), jaundice ($n = 49$) and dyspnea ($n = 49$). All patients showed some level of organic dysfunction: respiratory ($n = 51$), renal ($n = 46$), hepatic ($n = 45$), cardiovascular ($n = 35$), hematologic ($n = 32$) and neurologic ($n = 16$). The mortality rate was 40% ($n = 23$). The comparison from nonsurvivors with survivors showed that they have higher incidences of respiratory, cardiovascular and neurological failures as well as higher levels of acidosis ($P < 0.05$).
**Conclusions** In endemic regions leptospirosis has to be considered as a cause of multiple organic dysfunction with a high mortality rate mainly when respiratory, cardiovascular or neurological failures are present.

**References**

1. Ko AI, *et al.*: **Urban epidemic of severe leptospirosis in Brazil.** *Lancet* 1999, **354:**820-825.
2. Vieira S, Brauner J: **Leptospirosis as a cause of acute respiratory failure.** *Braz J Infect Dis* 2002, **6:**135-139.

## P32

## Combination of quinine and artesunate may be the best to prevent ARDS in Falciparum Malaria

**A Abraham**
*Breach Candy Hospital, Mumbai, India*
*Critical Care* 2005, **9(Suppl 1):**P32 (DOI 10.1186/cc3095)

The work was carried out in the intensive care unit of Parsee General Hospital, Mumbai 400036, India.
**Introduction** Falciparum Malaria is a dreaded parasitic infection, attacks all the organs in the human body cerebral, and chest dysfunction is very common in the infection followed by kidneys blood and so forth.
**Hypothesis** To study and compare the various treatment modalities and the attendant complications of Falciparum Malaria with or without concomitant Vivax in the intensive care unit. The study is done to find out the best treatment to offer to patients suffering with Facliparum Malaria infection and treat ongoing multiorgan failure and to prevent further complication of the dreaded parasitic infection.
**Methods** Retrospective study between 1993 and 1995 and prospective study from 1996 to 2003 of patients having severe malaria infection warranting intensive care management.
**Results** A total number of 181 patients. See Table 1.

**Table 1**

| Year | Number of patients | Died (ARDS + MOF) | Survived |
|---|---|---|---|
| 1993–1996 | 39 | 29 (no quinine) | 10 (quinine) |
| 1996 | 9 | 5 (no quinine) | 4 (quinine) |
| 1997 | 19 | 7 (no quinine) | 12 (quinine) |
| 1998 | 14 | 7 (no quinine) | 7 (quinine) |
| 1999 | 15 | 5 (no quinine) | 10 (quinine) |
| 2000 | 24 | 10 (no quinine) | 14 (quinine + artesunate) |
| 2001 | 34 | 1 (no quinine) | 33 (quinine + artesunate) |
| 2002 | 19 | 2 (no quinine) | 17 (quinine + artesunate) |
| 2003 until March | 8 | Nil | 8 (quinine + artesunate) |

ARDS, acute respiratory distress syndrome; MOF, multiorgan failure.

**Conclusions** (1) Quinine has given good and consistent results. Treatment must be initiated with quinine and must be given intravenously. (2) Parasites may have developed resistance to a multidrug regimen (mefloquine + others). (3) Quinine followed by artesunate 120 mg bolus followed by 60 mg daily intravenously for 5 days (quinine + artesunate together) yielded good results. This is the best that can presently be offered to patients with shock/multiorgan failure.

## P33

## Zygomycosis by Rhizopus species — a very rare angioinvasive mycosis: report of three cases

**J Lewejohann, M Hansen, C Zimmermann, P Kujath, H Bruch**
*Universitätsklinikum Schleswig-Holstein, Campus Lübeck, Denmark*
*Critical Care* 2005, **9(Suppl 1):**P33 (DOI 10.1186/cc3096)

**Introduction** Zygomycosis caused by Rhizopus species (Rhsp) is an aggressive and rapidly progressive opportunistic fungal infection in immunocompromised patients. It comprises mucocutaneous, rhinocerebral, pulmonary, urological and disseminated infections. Predisposing factors are immunosuppression owing to severe

diseases, immune defects or metabolic disturbances like diabetic ketoacidosis. Rhizopus infections are characterized by angioinvasive growth, necroses of infected tissue and perineural invasion. The invasion of blood vessels is remarkable for a fungal infection. The mortality of zygomycosis is very high, especially for disseminated disease and if immunosuppression cannot be corrected.

**Patients** *Patient 1* (female, 73 years): Delayed clinical course according to infection of a hip-TEP and a femoropopliteal bypass of the right leg, eventual exarticulation of the right hip joint, pseudomonas pneumonia, severe sepsis caused by staphylococci, acute respiratory distress syndrome, acute renal failure and multiple use of antibiotics. Subsequent detection of Rhsp in the bronchoalveolar lavage and treatment with amphotericin B for this reason. *Patient 2* (male, 68 years): Transplantation of kidney in past medical history, presenting with acute renal failure and with quite a few infections before. In the sequel development of abscessing pneumonia on the right side with a pleural empyema. Rhsp were detected by microbiological testing in the empyema fluid. These findings required surgical intervention, resection of the lower lobe of the right lung and, within the same operation, of the renal graft because of rejection. The patient was treated with Caspofungin because of Candidemia in addition to zygomycosis. The further course was delayed by several septic phases. *Patient 3* (male, 72 years): An insignificant past medical history with appendectomy, secondary wound-healing; hypertension, hyperlipoproteinemia. No hint for an immune defect. Operation because of adhesion ilueus, postoperative severe septic shock owing to peritonitis. After 1 month of intensive care therapy with multiple lavages and antibiotics microbiologically proven abdominal infection with Rhsp. All patients died later in spite of all efforts.

**Discussion** The very rarely seen zygomycosis caused by Rhsp developed in patient 1 and patient 2 owing to immunosuppression – in the first, iatrogenic induced by immunosuppressive drugs after organ transplantation; in the second as a result of previous immunosuppression and prolonged severe sepsis. Zygomycosis of the third patient developed because of prolonged severe septic shock without a hint of a immune deficit before.

In comparison with other mycoses, treatment of Rhsp infections remains difficult. The affinity to blood vessels, where the fungi multiply and their feature of vascular invasion with thrombosis and infarction are complicating therapeutic efforts, which should include surgical resection whenever possible and amphotericin B.

## P34

## A 16-year experience with toxic epidermal necrolysis

**E Dárdai, B Dede, M Telkes**
*St Stephen's General Hospital, Budapest, Hungary*
*Critical Care* 2005, **9(Suppl 1):**P34 (DOI 10.1186/cc3097)

Toxic epidermal necrolysis (TEN) is a devastating medication-induced extensive epidermal detachment with a reported mortality rate of 30–60% in adults. As in severe burns, fluid losses are massive, and superinfection, impairment of thermoregulation, excessive energy expenditure and alteration of immunologic functions are usual complications. Moreover, mucous membrane involvement increases morbidity. Previously reported data suggest that age, total body surface area (TBSA) involvement, late recognition and treatment of TEN are poor prognostic indicators.

The purpose of the clinical study was to evaluate the effects of special intensive and nutritional management on the outcome of patients with TEN.

Between 1988 and 2004 13 patients (five men, eight women, mean age 51 years) were admitted to our department. Two patients were in very poor condition at admission and died within 24 hours. They were excluded from the clinical study. Patients had a TBSA skin slough of 25–85% and a mean APACHE II score of 11.75.

Eleven patients were placed in a bacteria-controlled nursing unit, wounds were treated with topical debridement and antimicrobial medications. Nutritional therapy (enteral and/or parenteral) was instituted after fluid and electrolyte replacement. The daily caloric intake reached 146 kJ/kg body weight with a nitrogen–caloric ratio of 1:150. Enteral feeding (sip feeds, nasogastric tube, PEG) was forced as early as possible. One patient had diabetes mellitus (NIDDM).

With the complex treatment of 13–26 days in the ICU, nine patients recovered. Two patients died due to septic complications (infected central venous catheter, extended gastrointestinal mucousa involvement – mortality rate: 18%). In the last 8-year period all the patients with TEN healed, only one patient (86-year-old woman) died later due to acute myocardial infarction.

Our clinical experiences show that early recognition of TEN may decrease the morbidity and mortality. The local and general management of TEN should be carried out at an isolated, aseptic unit of an intensive care department. The conventional therapy combined with vigorous nutritional management may improve the patients survival. Our results for a group of older patients with TEN, with extensive skin and/or mucosal involvement suggest that age, a delay in proper hospitalisation, steroids and early empiric antibiotic treatment are associated with a poor prognosis.

## P35

## The removal of antibiotics during continuous venovenous hemofiltration (CVVH) in critically ill patients with acute renal failure: measured versus estimated CVVH clearance

**C Bouman, H Kan, M Schultz, M Vroom**
*Academic Medical Center, Amsterdam, The Netherlands*
*Critical Care* 2005, **9(Suppl 1):**P35 (DOI 10.1186/cc3098)

**Background** The clearance of antibiotics during continuous venovenous hemofiltration (CVVH) is calculated by multiplying the sieving coefficient (SC) (defined as the ratio of drug concentration in the ultrafiltrate to plasma) and the ultrafiltration rate (Quf). For most antibiotics the SC is unknown. It was suggested that the SC can be substituted by the non-protein-bound fraction (fu). However, fu values as reported in the literature are determined in healthy volunteers and not during critical illness. We compared measured and estimated CVVH clearance (ClCVVH) of five antibiotics.

**Methods** In 40 patients with ARF undergoing CVVH (predilution, cellulose-triacetate filter, Quf 36 ± 8 ml/min), prefilter, postfilter and ultrafiltrate samples were collected and drug concentrations were determined by HPLC or by immunoassay. The prefilter concentration (Cpre) was corrected using the dilution factor (Qb/Qb + Qinf), where Qb is the blood flow rate and Qinf is the substitution fluid infusion rate. The SC was calculated as follows: SC = 2 × Cuf / (Cpre + Cpost).

**Results** Data (mean ± standard deviation) are presented in Table 1. ClCVVH (ml/min) was calculated by multiplying the SC (or the fu) and the Quf.

**Table 1**

| Drug (*n*) | Measured SC | Measured ClCVVH | Non-protein-bound fraction | Estimated ClCVVH |
|---|---|---|---|---|
| Ceftazidim (4) | 2.14 ± 2.64 | 75 ± 92 | 0.79 | 28 ± 1 |
| Ciprofloxacine (16) | 0.89 ± 0.33 | 31 ± 12 | 0.60 | 21 ± 1 |
| Flucloxacilline (5) | 0.37 ± 0.38 | 13 ± 14 | 0.20 | 7 ± 0 |
| Fluconazol (9) | 0.86 ± 0.09 | 30 ± 2 | 0.88 | 31 ± 1 |
| Vancomycine (6) | 0.71 ± 0.19 | 27 ± 5 | 0.70 | 28 ± 9 |

SC, sieving coefficient; ClCVVH, continuous venovenous hemofiltration clearance.

**Conclusions** Measured and estimated ClCVVH corresponded well for fluconazol and vancomycine, but not for ceftazidim, ciprofloxacine and flucloxacilline, possibly due to changes in protein binding induced by critical illness or drug–membrane interactions. Therefore, for antibiotics with a narrow therapeutic range, monitoring drug concentrations remains mandatory.

## P36

### Ceftazidime reduces pulmonary hypertension in an ovine model of sepsis following smoke inhalation injury

**DM Maybauer[1], MO Maybauer[1], JF Fraser[2], LD Traber[1], P Enkhbaatar[1], N Morita[1], DL Traber[1]**
*[1]University of Texas Medical Branch, Galveston, TX, USA; [2]University of Queensland, Brisbane, Australia*
*Critical Care* 2005, **9(Suppl 1):**P36 (DOI 10.1186/cc3099)

**Objective** Our group recently developed an ovine model of *Pseudomonas aeruginosa* sepsis associated with acute lung injury (ALI) [1]. The aim of this study was to modify this model by the administration of Ceftazidime (Cef) to simulate a more clinically relevant situation. This modification could be the basis for future studies investigating new treatment strategies in sepsis.
**Methods** Eighteen sheep (35–40 kg) were operatively prepared for chronic study. After 7 days of recovery, sheep were randomly allocated either to sham, control, or Cef groups ($n = 6$ each). After a tracheostomy had been performed, ALI was produced in the control and Cef group by insufflation of 48 breaths of cotton smoke under deep halothane anesthesia. Then, live *P. aeruginosa* were instilled into the lungs via a bronchoscope [1]. The sham group received the vehicle, 48 breaths of room air and 30 ml saline. Subsequently, anesthesia was discontinued. The sheep were studied for 24 hours in the awake state and were ventilated with 100% oxygen (tidal volume 15 ml/kg, 30 breaths/min). The mean pulmonary artery pressure (MPAP) and pulmonary artery occlusion pressure (PAOP = wedge pressure) were determined every 3 hours. Cef (3 g, intravenously) was administered 1 hour and 13 hours post injury. The animals were resuscitated with Ringer's lactate solution to maintain filling pressures and hematocrit. Lung tissues were taken after the experiment to determine the bloodless lung tissue wet to dry weight ratio (W/D). Statistical analysis: two-way analysis of variance, Student–Newman–Keuls post hoc comparisons, significance $P < 0.05$.
**Results** MPAP and PAOP remained stable in sham animals. The control group showed a significant increase in MPAP (baseline [BL]: 19 ± 1 vs 24 hours: 31 ± 1) and PAOP (BL: 11 ± 1 vs 24 hours: 17 ± 1) versus BL over time. The Cef group also showed an increase in MPAP (BL: 20 ± 1 vs 24 hours: 26 ± 1) and PAOP (BL: 10 ± 1 vs 24 hours: 13 ± 1) vs BL, but this increase was significantly lower in comparison with the control group. The fluid balance (sham: −547 ± 38, control: +1266 ± 75, Cef: +382 ± 55) was significantly higher in the control and Cef groups compared with sham, but also significantly reduced in the Cef group compared with the control group. However, the W/D ratio after 24 hours (sham: 5.0 ± 0.1, control: 5.8 ± 0.2, Cef: 5.7 ± 0.2) increased significantly in the control and Cef groups compared with sham, but was not statistically different between those groups.
**Conclusion** The application of Cef after ALI associated with bacterial challenge reduced pulmonary hypertension and fluid requirement. The addition of antibiotics to the protocol will make it more clinically relevant and is a useful new approach for further studies in this modified sepsis model.
**Acknowledgements** Grant support from Shrine 8820, 8450, NIH GM066312.
**Reference**
1. Murakami, *et al.*: *Crit Care Med* 2002, **30:**2083-2090.

## P37

### Continuous versus intermittent infusion of temocillin in intensive care unit patients

**K Claeysoone, V Basma, R Hens, F Van Bambeke, R De Jongh, P Tulkens**
*ZOL, Genk, BE;UCL, Brussels, Belgium*
*Critical Care* 2005, **9(Suppl 1):**P37 (DOI 10.1186/cc3100)

**Background and goal** β-lactams are time-dependent antibiotics and show little gain in activity once their concentration exceeds the minimum inhibitory concentration about fourfold, which suggests their administration by continuous infusion. We have studied the stability, the compatibility with other drugs, and the pharmacokinetics of continuous or intermittent administration of temocillin (a β-lactam active against Gram-negative organisms).
**Methods** Temocillin was assayed by HPLC. Temocillin stability was measured over 24 hours after its solution in water at 37°C. Compatibility with several frequently used drugs on the ICU was determined under conditions mimicking their clinical use. Temocillin was measured in plasma samples from ICU patients with normal renal function, randomly assigned to receive a continuous ($n = 6$; 2 g every 12 hours; 5 day sample observation) or intermittent ($n = 6$; 2 g over 30 minutes twice daily; consecutive samples before and after dose 1 and 9) schedule.
**Results** Recovery after storage for 24 hours at 37°C of both R and S isomers of temocillin exceeded 90%, which is better among other studied β-lactams. Temocillin was compatible with most frequently used drugs on the ICU with the exception of clarithromycin, ciprofloxacin, meropenem, imipenem, piperacillin/tazobactam, vancomycin, amoxicillin/acid clavulanic acid, propofol, midazolam, piritramide, nicardipine, milrinone, and ranitidine. In patients with normal renal function, plasma levels of temocillin were above 50 mg/l in the continuous group, and 90% of the time above the breakpoint of 16 mg/l with peak levels of 120 mg/l after the first and ninth dose in the intermittent group.
**Conclusion** Temocillin can be used safely in the ICU, either with an intermittent or continuous schedule. The latter may be preferred based on pharmacodynamic considerations.

## P38

### Meropenem administration by intermittent infusion versus continuous infusion for the treatment of nosocomial pneumonia

**L Lorente, S Huidobro, M Martín, M Mora**
*Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain*
*Critical Care* 2005, **9(Suppl 1):**P38 (DOI 10.1186/cc3101)

**Objective** Mainly, beta-lactamic efficacy is determined by the duration of time that concentrations remain above the minimum inhibitory concentration (MIC). Some studies have found that the administration of carbapenems by continuous infusion maintain constantly concentrations above the MIC of susceptible organisms over the course of therapy; but limited data exist on clinical efficacy (only occasional observations have been made). The purpose of this study was to evaluate the clinical efficacy of meropenem by continuous infusion administration (CI) or by intermittent infusion (II) for the treatment of ventilator-associated pneumonia (VAP) caused by Gram-negative bacilli (GNB).
**Methods** An historic control group (1 July 2000–20 June 2002) with VAP caused by GNB who received initial empiric antibiotic therapy with meropenem by II ($n = 18$) was compared with a prospective cohort of patients (1 July 2002–30 June 2003) treated with meropenem by CI ($n = 10$), at a university hospital medical–surgical

ICU. VAP were treated during 14 days with two antibiotics: meropenem (1 g/6 hours intravenously) plus another (aminoglycoside or quinolone). Antibiotic clinical effect was categorized as cure or failure. Differences between groups were tested by means of Student's *t* test and exact chi-square by permutation, using Statxact Software 5.0. We consider values $P < 0.05$ as a significant difference.
**Results** Significant differences were not found between both groups of patients (15 with CI and 30 with II) in sex, age, APACHE II score, diagnosis, microorganism responsible and organ dysfunction severity assessed by the Sepsis-related Organ Failure Assessment score. The CI group showed significantly greater clinical cure than the II group (CI, 14/15 [93.33%] vs II, 19/30 [63.33%], $P = 0.038$) and smaller, but not significant, attributable mortality to VAP (1 of 15 [6.66%] vs 7 of 30 [23.33%], $P = 0.236$).
**Conclusions** Our data suggest that administration of meropenem by CI may have more clinical efficacy than administration by II for the treatment of nosocomial pneumonia, but more studies are required to confirm it.

## P39

### Continuous infusion versus intermittent infusion of ceftazidime for the treatment of pneumonia caused by *Pseudomonas aeruginosa*

**L Lorente, C García, M Martín, M Mora**
*Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain*
*Critical Care* 2005, **9(Suppl 1):**P39 (DOI 10.1186/cc3102)

**Objective** Beta-lactamics antibiotics exhibit concentration-independent bactericidal activity. Several studies have found that ceftazidime by continuous infusion appears to optimise the pharmacodynamic profile by constantly providing concentrations in excess of the minimum inhibitory concentration of susceptible organisms over the course of therapy. Limited data exist on clinical efficacy by continuous infusion of ceftazidime. The purpose of this study was to evaluate the clinical efficacy associated with the administration of continuous infusion of ceftazidime (CI) and intermittent infusion of ceftazidime (II) for the treatment of ventilator-associated pneumonia (VAP) caused by *Pseudomonas aeruginosa*.
**Methods** An historic control group (1 July 2000–20 June 2002) with VAP caused by *P. aeruginosa* who received initial empiric antibiotic therapy with ceftazidime by II ($n = 32$) was compared with a prospective cohort of patients (1 July 2002–30 June 2003) treated with ceftazidime by CI ($n = 15$), at a university hospital medical–surgical ICU. Patients were treated during 14 days with ceftazidime, by CI (4 g/day) or II (2 g/8 hours), plus tobramycin. Exclusion criteria was creatinine clearance < 60 ml/mn. Antibiotic clinical effect was categorized as cure or failure. Differences between groups were tested by means of Student's *t* test and exact chi-square by permutation, using Statxact Software 5.0.
**Results** Significant differences were not found between both groups of patients (eight with CI and 12 with II) in sex, age, APACHE II score, diagnosis and organ dysfunction severity assessed by the Sepsis-related Organ Failure Assessment score. The CI group showed greater clinical cure rate than the II group (8 of 8 [100%] versus 4 of 12 [33.33%], $P = 0.004$) and smaller atributable mortality to VAP (0 of 8 [0%] versus 6 of 12 [50%], $P = 0.024$). In addition, CI patients received one-third less daily dose than those treated by II.
**Conclusions** These data suggest that ceftazidime administration by continuous infusion may have more clinical efficacy that intermittent infusion, in treatment of VAP caused by *P. aeruginosa*.

## P40

### Laparostomy versus laparotomy in severe abdominal infection: microbiological assessment

**V Pavoni, L Gianesello, L Paparella, G Gori, G Gritti**
*Az. Ospedaliera Careggi Firenze, Italy*
*Critical Care* 2005, **9(Suppl 1):**P40 (DOI 10.1186/cc3103)

**Introduction** Mortality of severe abdominal infection, due to peritonitis after anastomotic dehiscence, visceral organ necrosis or necrotic pancreatitis, remains high. The efficacy of laparostomy in damage control surgery and uncontrolled intra-abdominal infection is controversial [1].
**Methods** We retrospectively reviewed the records of all patients with severe abdominal infection secondary to peritonitis admitted to the ICU of a university teaching hospital from 1998 to 2000. The following information was collected: age, simplified acute physiology score (SAPS II) and sepsis-related organ failure assessment (SOFA) on admission, length of stay (LOS), ICU and hospital outcome, type of bacteria, number of isolations and haematogenous dissemination.
**Results** Thirty-nine critically ill patients were studied. The mean age was 66.1 ± 16.9; the overall SAPS II at admission was 41.7 ± 14.6; the SOFA was 10.9 ± 4.3. A total of 13 laparostomy were performed (group I). Twenty-six patients were undergoing a laparotomy (group II). No differences regarding age (group I vs group II 61.1 +± 12.7 vs 68.5 ± 18.1, $P = 0.08$), SAPS II (41.8 ± 20.6 vs 41.5 ± 10.6, $P = 0.65$) and SOFA (11.8 ± 5.5 vs 10.4 ± 3.5, $P = 0.49$) were found. The duration of ICU stay was longer in group I than in group II (44.4 ± 52.2 vs 19.8 ± 17.3, $P = 0.04$). ICU mortality was equal between two groups (30.7%). Hospital mortality was not statistically different between two groups (38.4% vs 42.3%, $P = 0.77$). The number of positive cultural specimens was 19 in both groups. Isolated microorganisms were: Gram-positive cocci (21% vs 26.3%), *Pseudomonas aeruginosa* (26.4% vs 31.6%), other non-fermenting Gram-negative bacilli (21% vs 10.5%), Enterobacteriaceae (16% vs 10.5%), fungi (15.8% vs 15.8%). Two of five *P. aeruginosa* isolations in Group I were multiresistant to available antibiotics and sensible only to combinations. Four out of 13 patients in group I presented candidemia compared with two of 26 patients in group II. Haematogenous dissemination was greater in group I (85.7% vs 50%).
**Conclusions** The laparostomy technique used in the management of severe intra-abdominal sepsis appears to correlate with significant ICU stay and costs. Prolonged antibiotic therapy and frequent intra-abdominal procedures determine higher incidence of infections caused by Gram-negative, enterobacteriaceae and multiresistant pseudomonaceae. The incidence of fungal infection is not influenced by surgical approach, but the 'open abdomen' strategy seems to facilitate dissemination.

**Reference**

1. Wittmann DH, Schein M, *et al.*: **Management of secondary peritonitis.** *Ann Surg* 1996, **224:**10-18.

## P41

### Logistic regressive analysis of potential prognostic factors for pulmonary complications after abdominal surgery in elderly patients

**XR Wang, Y Gao, YJ Zheng, J Chen, Y Deng, Y Hang, D Sun**
*Department of Anesthesiology, Renji Hospital, Shanghai Second Medical University, Shanghai, China*
*Critical Care* 2005, **9(Suppl 1):**P41 (DOI 10.1186/cc3104)

To investigate potential prognostic factors and to predict extent of risks for postoperative pulmonary complications by logistic

regressive analysis, and to evaluate the role of non-invasive ventilation in reducing the incidence of complications in elderly patients. A stair-climbing test was carried out with ASA score, FEV1, changes of $SpO_2$ and HR noted at the same time. Logistical regressive analysis based on these parameters were used to assess the relation between potential prognostic factors and postoperative complications. Patients with limited pulmonary reserves were selected using the equation, and the protective effect of non-invasive ventilation on these patients was assessed. The incidence of postoperative pulmonary complications for high-risk patients with non-invasive ventilation was 33.2%, and the incidence of pulmonary complications for high-risk patients without non-invasive ventilation was 67.7%. There was not a significant difference between these two groups with low-risk ($P > 0.05$). The mathematical model of logistic regressive analysis using the stair-climbing testing combined with other parameters is a simple, reliable method to predict the cardiopulmonary reserved function in elderly patients. Non-invasive ventilation can effectively reduce the incidence of postoperative pulmonary complications for high-risk patients, but it has no effect on patients with low risk.

## P42

### Bariatric surgery postoperative management: complications in a series of 278 patients admitted to an intensive care unit

**M Knibel, F Muller, R Hatum, C Roderjan, E Guimarães, M Lugarinho, C Vasconcelos, A Vanzan, M Mattos**
*Sao Lucas Hospital, Rio De Janeiro, Brazil*
*Critical Care* 2005, **9(Suppl 1):**P42 (DOI 10.1186/cc3105)

**Introduction** Morbid obesity is one of the most important public health problems these days, and bariatric surgery became an option to patients with body mass index of 35 or higher and obesity-related complications (hypertension, diabetes, etc.).
**Patients and methods** We observed the postoperative period of these patients in our ICU during 10 months ($n = 278$) and their possible postoperative complications.
**Results** Found were athelectasy in 60%, surgical wound minor bleeding in 2.5%, pulmonary embolism in 0.35%, pneumonia in 1.43%, acute renal failure in 1.07%, rhabdomyolisis in 2.8%, peritonitis in 1.43%, respiratory failure in 2.5%, acute respiratory distress syndrome in 1.07%, cardiac arrhythmia in 1.43%, gastro-intestinal fistula in 2.5%, acute myocardial infarction in 0.72%, lower gastrointestinal hemorrhage in 0.71%, and bowel obstruction in 0.71%. The death overall rate was 1.43%.
**Conclusions** The most common postoperative complication was athelectasy, showing the need for a respiratory therapist at the bedside to perform non-invasive mechanical ventilation in the immediate postoperatorium period. Peritonitis was the worst complication, accounting for all deaths; the intensive care team must be prepared to immediately recognize and manage these cases. The results are in accord with those found in the recent medical literature.

## P43

### The role of the Shuttle Walking Test in predicting mortality and morbidity post oesophagogastric surgery

**P Whiting, P Murray, S Hutchinson, C Stoddard, R Ackroyd**
*Sheffield Teaching Hospitals, Sheffield, UK*
*Critical Care* 2005, **9(Suppl 1):**P43 (DOI 10.1186/cc3106)

**Introduction** The Shuttle Walking Test (SWT) has been previously shown to correlate well with patients' maximal oxygen uptake ($VO_2$ max) [1–3]. Older and colleagues demonstrated that an anaerobic threshold of 911 ml/min/kg, in patients undergoing major abdominal surgery, was an excellent predictor of mortality from cardio-respiratory causes [4]. Patients undergoing oesophagogastric surgery currently have a 30-day mortality of approximately 9% in our institution and are all admitted to critical care postoperatively. Our aim was to assess the value of a preoperative SWT in trying to identify high-risk patients.
**Method** All patients listed for oesophagogastrectomy between April 2002 and September 2004 undertook a SWT as a standard part of their preoperative assessment. Routine anaesthesia, surgery and critical care was provided guided by clinical requirements. Thirty-day mortality was compared retrospectively with shuttle test data.
**Results** Thirty-nine patients undertook a SWT, and had surgery. The mean age of the group was 64 years (range 44–81 years). The mean SWT distance was 480 m (range 220–880 m). At the 30th postoperative day, 18 patients had been discharged home (46.2%), 14 patients remained on the wards (35.9%), three still required critical care (7.7%) and four patients had died (10.2%). No patient with a SWT of greater than 350 m died within 30 days of surgery. Patients with a SWT of 350 m and below had a 50% 30-day mortality.
**Discussion** This small patient group appears to be representative of the oesophagogastric surgical population within our institution (mortality 10.2% vs 9%). A SWT of 350 m appears to be a sensitive marker of increased postoperative mortality in this particular patient population. This finding is consistent with Lewis and colleagues' [2] data correlating SWT distance with $VO_2$ max and Older and colleagues' [4] work on the anaerobic threshold and perioperative outcome. Further evaluation is required, but using this simple, cheap and reliable non-invasive preoperative test may help to risk-stratify patients undergoing high-risk surgery. High-risk groups may benefit from appropriately informed consent for surgery but potentially also from preoperative cardiopulmonary training and a focused utilisation of resources.
**References**
1. Morales FJ, *et al.*: *Am Heart J* 1999, **138:**291-298.
2. Lewis ME, *et al.*: *Heart* 2001, **86:**183-187.
3. Singh SJ, *et al.*: *Eur Resp J* 1994, **7:**2014-2020.
4. Older P, *et al.*: *Chest* 1999, **116:**355-362.

## P44

### Prospective, randomized trial comparing fluids and dobutamine optimization of oxygen delivery in high-risk surgical patients

**S Lobo, F Lobo, C Polachini, D Patini, K Andraus, A Yamamoto, P Alvarez, H Sanchez, M Queiroz, S Teixeira, P Serrano, A Christiano Jr, E Sivieiro, M Spegiorin, G Cunrath, N Oliveira**
*Famerp – Hospital de Base, Sao José do Rio Preto, Brazil*
*Critical Care* 2005, **9(Suppl 1):**P44 (DOI 10.1186/cc3107)

**Introduction** Preventing perioperative tissue oxygen debt contributes to a better postoperative recovery. Whether the beneficial effects of fluids and inotropes during optimization of oxygen delivery ($DO_2$) in high-risk surgical patients are due to fluids, inotropes or the combination of the two is not known. We aimed to investigate the effect of fluid optimization, without the use of inotropes, on morbidity.
**Methods** A randomized controlled trial with pulmonary artery catheter (PAC)-guided haemodynamic optimization in 50 high-risk patients (elderly with coexistent pathologies) undergoing major elective surgery. Therapy consisted of optimization during the operation and 24 hours postoperatively using either fluids alone ($n = 25$) or fluids and dobutamine ($n = 25$), aiming to achieve supranormal values ($DO_2 > 600$ ml/min/m$^2$). Clinical complications such as pulmonary edema and/or heart failure, acute myocardial

infarction, bleeding, thrombosis, fistula and acute renal failure were monitored.

**Results** Prevalence of pulmonary edema/heart failure significantly increased in the fluid optimization group in comparison with the dobutamine optimization group in the postoperative period (40% vs 12%, relative risk [RR] 3.33, 95% confidence interval [CI] 1.04–10.7, respectively, $P < 0.05$). Clinical complications were more frequent in the fluid optimization group than in the dobutamine group (68% vs 28%, RR 2.43, 95% CI 1.22–4.81, $P < 0.05$). The 30-day mortality rates were 8% in dobutamine optimization group and 20% in the fluid optimization group (RR 2.5, 95% CI 0.53–11.70, not significant).

**Conclusion** In high-risk patients undergoing major surgery, PAC-guided hemodynamic optimization using dobutamine determines better outcomes, whereas fluids alone increase the incidence of postoperative complications.

## P45

### Early goal directed therapy reduces morbidity and length of hospital stay following high-risk surgery

**R Pearse, D Dawson, J Fawcett, A Rhodes, M Grounds, D Bennnett**
*St George's Hospital, London, UK*
*Critical Care* 2005, **9(Suppl 1):**P45 (DOI 10.1186/cc3108)

**Introduction** Several studies have described the successful use of goal directed therapy to guide fluid and inotropic therapies in patients at high risk of postoperative complications. This has mainly been performed in either the pre-operative or intra-operative period. It is unclear whether this is effective solely in the postoperative period. The aim of this study was to evaluate the effect of an early goal directed therapy (EGDT) protocol that does not utilize the pulmonary artery catheter, when commenced immediately after general surgery in patients at high risk of complications.

**Methods** A prospective, randomized controlled trial in high-risk surgical patients on a general ITU. Patients were randomized to conventional treatment or EGDT for 8 hours immediately following surgery. The goals for EGDT were to optimize volume status by maximizing stroke volume with fluid challenges and then to increase the oxygen delivery index ($DO_2I$) to 600 ml/min/m$^2$ with dopexamine if required. Control group patients received fluid guided by central venous pressure. Other therapeutic targets were the same for both groups. Stroke volume and $DO_2I$ were measured in both groups using lithium indicator dilution and pulse contour analysis (LiDCOplus system). Postoperative complications were predefined and patients were followed up for 60 days. Data are presented as medians ± standard error or percentage.

**Results** One hundred and twenty-two patients (control = 60, EGDT = 62) were randomized. There were no significant differences between the two groups at baseline. Most patients underwent gastrointestinal, vascular or urological surgery. Patients in the EGDT group subsequently achieved higher $DO_2I$ than controls ($P < 0.0001$) and more EGDT patients achieved a $DO_2I$ of 600 ml/min/m$^2$ (82% vs 42%, $P < 0.0001$). The $DO_2I$ target was achieved as a result of increases in both stroke volume ($P = 0.02$) and heart rate ($P < 0.0001$). The EGDT group received more intravenous fluid (3015 ± 146 ml vs 2280 ± 164 ml, $P = 0.0006$) and more EGDT patients received dopexamine (89% vs 2%, $P < 0.0001$). The EGDT group developed fewer complications (0.7 vs 1.5 per patient, $P = 0.002$) and had a shorter hospital stay (11 ± 3 days vs 14 ± 5 days, $P = 0.002$). Infectious complications in the EGDT group were half that of the control group (24 episodes vs 49 episodes, $P = 0.0004$). The EGDT group utilized 640 less hospital bed-days. There was no difference in 28-day (9.7% vs 10%) or 60-day (11.3% vs 11.7%) mortality.

**Discussion** EGDT immediately following general surgery in high-risk patients reduces complications and length of hospital stay. This approach is both practical and effective.

## P46

### Impact of a low postoperative central venous oxygen saturation on postoperative morbidity

**J Divatia, V Priya, R Shingade**
*Tata Memorial Hospital, Mumbai, India*
*Critical Care* 2005, **9(Suppl 1):**P46 (DOI 10.1186/cc3109)

**Background** Patients undergoing major surgery have an increased oxygen debt that may affect postoperative outcomes. Current strategies of perioperative hemodynamic optimisation necessitate use of a pulmonary artery catheter. In patients with severe sepsis, early goal directed therapy using a central venous catheter and targeted to $ScvO_2$ of 70% improves survival. This strategy is untested in perioperative patients.

**Aim** To investigate whether a low postoperative $ScvO_2$ is associated with increased postoperative morbidity.

**Methods** Observational study from August to December 2003 in a 22-bed ICU-HDU of a tertiary referral cancer centre. $ScvO_2$ was analysed from blood collected from a central venous catheter at 2 and 12 hours after surgery in 83 patients undergoing major resections for cancer. Patients were divided into two groups: normal ($ScvO_2 \geq 70\%$ at both intervals) and low ($ScvO_2 < 70\%$ at one or both intervals). Central venous pH and base excess were also noted. The ICU team managing clinical care was unaware of the $ScvO_2$ values. Outcomes studied were ventilator days, length of ICU and hospital stay, ICU and hospital mortality, incidence of anastomotic leak and incidence of complications (any of sepsis, cardiovascular or respiratory complications, ICU stay ≥ 2 days or ventilator days ≥ 2 days). Data were analysed using the unpaired *t* test and chi-square test. Binary logistic regression (stepwise forward conditional) was performed to determine the parameters contributing to morbidity.

**Results** Fifty-one patients (62%) had a low $ScvO_2$ at one or both time intervals. Patients in the low group had significantly lower $ScvO_2$ at 2 hours (63.9 ± 8.9 vs 76.8 ± 5.8, $P = 0.000$) and 12 hours (68.7 ± 6.1 vs 76.2 ± 4.1, $P = 0.000$), respectively. APACHE II scores within 24 hours of ICU admission were similar (8.9 ± 2.7 vs 9.9 ± 2.7, $P = 0.1$). There was no difference in ICU or hospital mortality (both 3 vs 0, $P = 0.16$) between the low and normal groups, respectively. pH and base excess were not different. Patients in the low group had more days on ventilator (3.5 ± 6.1 days vs 0.59 ± 1.5 days, $P = 0.009$), and longer ICU stay (5.6 ± 6.7 days vs 1.75 ± 2.6 days, $P = 0.009$) and hospital stay (17.8 ± 10.5 days vs 13.7 ± 5.06 days, $P = 0.002$). They required more colloid infusion postoperatively (682 ± 398 ml vs 228.4 ± 279 ml). There was no difference in the number of patients requiring inotropes (1 vs 0, $P = 0.1$). Significantly more patients in the low group developed postoperative complications (56.8% vs 18.7%, $P = 0.009$) and anastomotic dehiscence (26% vs 9%, $P = 0.03$). On logistic regression, only $ScvO_2$ at 12 hours ($P = 0.012$) affected morbidity.

**Conclusions** A low $ScvO_2$ was associated with major post-operative morbidity. The results of this observational, hypothesis-generating study justify a prospective trial of perioperative goal directed therapy.

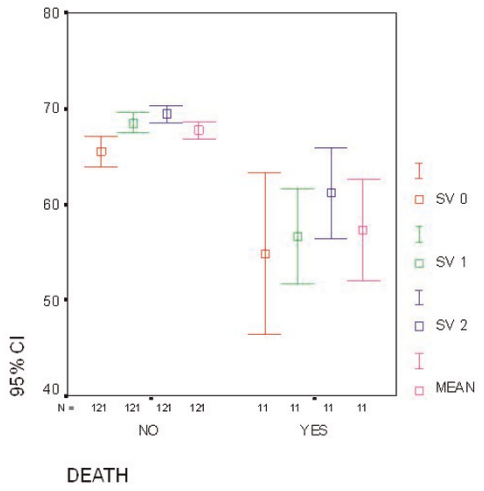
## P47

### Can central venous oxygen saturation intermittently measured within the first 24 postoperative hours of cardiac surgery predict death?

**P Matos Nogueira[1], R Vieira Gomes[1], A Rouge[1], M Fernandes[1], B Tura[1], J Rocco[2], L Almeida Campos[1], H Rocha Dohmann[1], A Melo[1], F Graça Aranha[1], J Sabino[1]**
*[1]Pró-Cardíaco, Rio de Janeiro, Brazil; [2]Hospital Clementino Fraga Filho, Rio de Janeiro, Brazil*
*Critical Care* 2005, **9(Suppl 1):**P47 (DOI 10.1186/cc3110)

**Background** Central venous oxygen saturation ($ScVO_2$) has been considered an important parameter for follow-up, prognostic estimate, and therapeutic target in the management of critically ill patients.
**Objective** To analyze the impact of $ScVO_2$ on the postoperative period of cardiac surgery, and to correlate it with inhospital death. Three $ScVO_2$ measurements were taken within the first 24 postoperative hours, and the overall mean was calculated.
**Case series and methods** A classic cohort of 132 consecutive patients selected from January 2004 to August 2004 and divided into the following two groups: Group I, death ($n = 11$, 8.3%); and Group II, survivors. Blood samples were collected through a central venous catheter properly positioned in the right atrium according to a previously validated method. The $ScVO_2$ measurements were taken in the postoperative period as follows: immediately (SV0), after 6 hours (SV1), and after 24 hours (SV2). A mean of the three measurements was calculated (mSV). Inhospital mortality was the occurrence of death during hospitalization. The Student *t* test was used for statistical analysis.
**Results** The mean $ScVO_2$ values of Group I compared with those of Group II were as follows, respectively: SV0, 54.8% ± 12.6 vs 65.4% ± 8.9 ($P < 0.0001$); SV1, 56.6% ± 7.3 vs 68.5% ± 5.9 ($P < 0.001$); SV2, 61.1% ± 7 vs 69.3% ± 5.3 ($P < 0.001$); and mSV, 57.3% ± 7.8 vs 67.7% ± 4.9 ($P < 0.001$). The distribution of variation of $ScVO_2$ was normal. The EuroScore was as follows: in the total sample, 5.3 ± 3.6; in Group I, 8.7 ± 6.1; and in Group II, 5 ± 3.1 ($P = 0.001$). The predicted mortality was around 11%, and the inhospital mortality was 8.3%.
**Conclusions** In the population studied, a lowest $ScVO_2$ measured within the first 24 postoperative hours and the EuroScore were related to inhospital death.

**Figure 1 (abstract P47)**




## P48

### Central venous saturation as a weaning success predictor

**C Teixeira, S Vieira, N Silva, L Savi, L Nasi, J Horer, R Oliveira, T Tonietto, R Wickert, R Cremonese, S Brodt, E Oliveira, F Alves, J Barth, C Trevisan, F Callefe, K Pinto, K Hartmann, L Borges**
*Moinhos De Vento Hospital, Porto Alegre, Brazil*
*Critical Care* 2005, **9(Suppl 1):**P48 (DOI 10.1186/cc3111)

**Introduction** The frequently used parameters to predict weaning failure (WF) from mechanical ventilation (MV) weaning parameters have low predictive capacity. Although being the most common cause of WF, early detection of respiratory muscle fatigue is difficult. Central venous saturation ($ScvO_2$) is a marker of oxygen consumption and could be applied for detection of WF.
**Objective** To evaluate the predictive capacity of $ScvO_2$ in detecting WF or success.
**Design** A prospective observational clinical multicentric study in three ICUs of Porto Alegre.
**Methods** Between August 2003 and December 2004, all patients with more than 48 hours of MV, in the weaning process, were submitted, after informed consent, to a spontaneous breathing trial (SBT) of 30 min and followed during the next 48 hours. All patients in the trial had arterial and venous gas analysis, and hemodynamic (cardiac rate, systolic and diastolic pressure) and ventilatory parameters (respiratory rate, tidal volume, f/VT index and maximal inspiratory pressure) during the MV time and in the 30th minute of SBT. The outcomes were reintubation and mortality rates.
**Results** Sixty-three MV patients were included, 55.5% male, mean age 55.8 ± 18.6 years, APACHE II score 18.2 ± 6.3. Septic shock was the most frequent diagnosis with 50.8% of cases; mortality ICU rate in the period 22.2%; weaning failure with reintubation rate 31.7% and mortality higher in WF patients (75% vs 14%, $P < 0.001$). $ScvO_2$ at the 30th minute of SBT was lower in WF patients (58.2 ± 7.1 vs 66.3 ± 5.4, $P = 0.003$). Hemodynamic and mechanic ventilatory parameters were not able to predict WF or mortality. The $PaO_2$, $SaO_2$ and $ScvO_2$ values dropped comparing the MV time and the 30th minute of SBT (110.1 ± 39.8 vs 95.8 ± 28.8, $P < 0.01$; 97 ± 2.4 vs 95.3 ± 3.7, $P < 0.001$; and 68.3 ± 7.3 vs 64.6 ± 8.6, $P < 0.001$, respectively). WF patients had the most accentuated fall in these parameters (102.1 ± 38.5 vs 85.8 ± 20.1, $P = 0.008$; 96.9 ± 2.7 vs 94.2 ± 3.9, $P = 0.001$; and 68.2 ± 7.4 vs 59.5 ± 7.3, $P < 0.001$, respectively).
**Conclusion** The reduction of $ScvO_2$ values during SBT is correlated with the outcome reintubation. This is probably due to an increase in oxygen muscle consumption and not only correlated to changes in oxygen muscle offer.

## P49

### Effects of optimizing cardiac output by fluid loading on the indocyanine green plasma disappearance rate and splanchnic microcirculation

**S Sakka, D Hofmann, O Thuemer, C Schelenz, K Reinhart**
*Friedrich-Schiller-University of Jena, Germany*
*Critical Care* 2005, **9(Suppl 1):**P49 (DOI 10.1186/cc3112)

**Introduction** Hypovolemia may be associated with splanchnic hypoperfusion and reduced in liver blood flow and function. In general, optimizing the cardiac preload to increase the cardiac output – a major determinant of systemic oxygen delivery – is a primary clinical goal. In this study, we tested the hypothesis that increasing the cardiac output by optimizing the intravascular fluid status leads to an improved regional (i.e. hepato-splanchnic) blood flow and function as assessed by the indocyanine green plasma

disappearance rate (ICG-PDR), which has been shown to be of major prognostic relevance [1].

**Methods** With approval by our ethics committee and written patient consent we prospectively studied 12 postoperative cardiac surgical patients (mean age 66 ± 13 years) who underwent elective coronary artery bypass grafting. All patients underwent extended hemodynamic monitoring by a pulmonary artery and left atrial catheter for clinical indication. Microcirculation within the splanchnic area was assessed by gastric tonometry, and liver blood flow and function were determined non-invasively by transcutaneous measurement of ICG-PDR. All these patients who were considered hypovolemic underwent hemodynamic optimization by infusion of hydroxyethylstarch (130 kDa). Global and regional parameters were measured at baseline and 1 hour after fluid challenge. All patients received pressure-controlled mechanical ventilation and respirator settings remained unchanged throughout the study. Data are expressed as mean ± standard deviation. For statistical analysis, a paired *t* test was used and $P < 0.05$ was considered significant.

**Results** Overall, 630 ± 130 ml hydroxyethylstarch were administered. In all patients, the cardiac index significantly increased following fluid administration, on average from 2.8 ± 0.7 to 3.6 ± 0.6 l/min/m$^2$ and the stroke volume index from 30 ± 7 to 38 ± 8 ml/m$^2$, respectively. With respect to cardiac preload, the central venous pressure significantly increased from 6 ± 2 to 12 ± 2 mmHg and the left atrial pressure from 5 ± 3 to 11 ± 3 mmHg, respectively. However, the ICG-PDR and $PCO_2$ gap (difference between gastric mucosal and end-tidal $CO_2$ tension) did not change significantly (i.e. from 21.2 ± 6.5 to 21.6 ± 6.5%/min and from 0.9 ± 0.5 to 1.0 ± 0.7 kPa).

**Conclusion** Optimizing cardiac output by fluid loading *per se* is not associated with a significant change in ICG-PDR or gastric mucosal $PCO_2$. However, since ICG-PDR in all patients with a value <18%min increased, we hypothesize that particularly patients with an *a priori* low ICG-PDR may benefit from optimizing cardiac index by fluid loading. Further studies are needed to test this hypothesis.

**Reference**

1. Sakka SG, Reinhart K, Meier-Hellmann A: **Prognostic value of the indocyanine green plasma disappearance rate in critically ill patients.** *Chest* 2002, **122:**1715-1720.

## P50

## Carbon dioxide output in septic shock

**V Pilas, N Vucic, K Cala**
*GH Sveti Duh, Zagreb, Croatia*
*Critical Care* 2005, **9(Suppl 1):**P50 (DOI 10.1186/cc3113)

**Introduction** Tissue hypoperfusion with concomitant hypoxia is a leading sign of septic shock. Despite increased $DO_2$ after volume administration, $VO_2$ remains low. Our hypothesis was that in this setting, lower $CO_2$ output would also occur. We calculated anaerobic output of $CO_2$ and found its small proportion to complete $CO_2$ output.

**Methods** We measured the output of $CO_2$ as well as the venous–arterial difference in $CO_2$ concentration (v–a$DCO_2$) in 25 patients in septic shock. All patients were mechanically ventilated, and the circulatory volume and pressure variables were monitored and changed according to pulmonary catheter findings.

$CO_2$ output was measured by use of our own technical innovation; a 5 l balloon was placed on the expiratory outlet and the $CO_2$ concentration was measured by standard capnograph. Minute ventilation was measured by a volume monitor over an ascending and a descending line.

**Results** In 10 survivors $VCO_2$ was higher than in nonsurvivors at the baseline (189 ± 10 vs 173 ± 14, $P = 0.0005$). The cardiac index was also higher (3.1 ± 0.27 vs 2.7 ± 0.6, $P = 0.03$). There was no significant difference in v–a$DCO_2$ (7.3 ± 1.6 vs 7.3 ± 1.4, $P = 0.95$).

During resuscitation $VCO_2$ increased markedly in survivors ($P = 0.0004$), whereas in nonsurvivors only an increasing trend was noted, but it did not reach statistical significance ($P = 0.12$).

**Conclusion** We conclude that this simple and noninvasive test of measurement of $VCO_2$ in patients in septic shock may be useful in early detection of metabolic disarrangements caused by hypoxia, as well as outcome of disease. It may also be used as a measure of treatment efficiency.

## P51

## What effect of vasoactive drugs on passive leg raising response in critically ill patients?

**S Alaya, S Abdellatif, H Ksouri, R Nasri, H Ghadhoun, O Béji, H Neffati, Y Sellami, S Ben Lakhal**
*Rabta Hospital, Tunis, Tunisia*
*Critical Care* 2005, **9(Suppl 1):**P51 (DOI 10.1186/cc3114)

**Introduction** Passive leg raising (PLR) mimics the hemodynamic effects of rapid fluid loading (FL) by shifting venous blood from the legs towards the intrathoracic compartment and by increasing right and left ventricular preloads.

**Aim** To test the effect of vasoactive drugs on PLR response.

**Patients and methods** During a period of 2 months (September–November 2004) were enrolled all patients with sepsis or septic shock under mechanical ventilation who needed FL. The hemodynamic measures include heart rate, invasive arterial pressure, pulse pressure (PP), venous central pressure in a supine position and after leg raising (45°); before and immediately after FL of 300 ml saline solution.

**Results** Twenty-eight hemodynamics measures were made. All patients were mechanically ventilated and deeply sedated. Age 55 ± 18 years, SAPS II 37 ± 17. The patients were divided into two groups.

Group 1 (with vasoactive drug): nine measures, age 58 ± 15 years, SAPS II 48 ± 26. The increase of PP after PLR is 4 ± 2.7 mmHg, while the increase of PP after FL is 5 ± 3 mmHg.

Group 2 (without vasoactive drug): 19 measures, age 54 ± 19 years, SAPS II 33 ± 10. The increase of arterial PP after PLR is 10 ± 8 mmHg while the increase of PP after FL is 8.3 ± 7 mmHg.

**Discussion** PLR predicts the effect of FL in all patients. It depends in part on the volume of blood contained in the leg vessels. The PP increase after PLR is more important in patients without vasoactive drugs (10 ± 8 vs 4 ± 2.7 mmHg).

**Conclusion** PLR is a very simple technique to predict the effect of FL. Its effects seem to be less important in patients with vasoactive drugs.

## P52

## Respiratory variation of plethysmography signal with a pulse oxymeter: new predictive parameters of fluid responsiveness?

**M Feissel[1], J Badie[1], K Bendjelid[2], I Mangin[1], G Robles[1], O Ruyer[1], J Faller[1], J Teboul[3]**
*[1]Centre Hopital Général, Belfort, France; [2]Geneva University Hospital, Geneva, Switzerland; [3]CHU Bicètre, Kremlin Bicètre, France*
*Critical Care* 2005, **9(Suppl 1):**P52 (DOI 10.1186/cc3115)

**Introduction** Respiratory variation of pulse pressure (ΔPP) and of time of pre-ejection (ΔPEP) obtained from an arterial catheter have been shown as reliable predictors of fluid responsiveness in

mechanically ventilated patients on sinus rhythm. The curve of plethysmography obtained from a pulse oximeter allows one to calculate respiratory variation of 'pulsed plethysmography' (ΔPlethP) and of pre-ejection time (ΔPEPPleth).

**Aim** To examine whether ΔPlethP and ΔPEPPleth could predict volume responsiveness as well as ΔPP and ΔPEP calculated from an arterial catheter.

**Patients** Nineteen patients with septic shock, fully adapted to the ventilator and on sinus rhythm, were studied before and after a fluid challenge.

**Methods** Pulsed plethysmography was defined by the amplitude of the pulse oximeter wave. The pre-ejection period was defined by the time between the onset of the QRS and the onset of the blood pressure curve for PEPKT and the onset of the plethysmography curve for PEPPleth. The ECG, blood pressures and plethysmography tracings were recorded simultaneously on a computer. The respiratory variation of the parameters were calculated and averaged from five respiratory cycles according to the following formula: $\Delta P = [P\max - \min / P\max + \min / 2] \times 100$. Responders were defined as patients who increased their cardiac output – measured by Doppler transthoracic echocardiography – by more than 15% after fluid challenge.

**Results** A strong correlation between the baseline value of the studied indices and the changes in cardiac output was observed ($r = 0.86$ and 0.85 for ΔPPKT and ΔPEPKT and $r = 0.82$ for both ΔPPPleth and ΔPEPPleth). Table 1 confirms the reliability of ΔPPKT and ΔPEPKT to discriminate responders from non-responders. It also shows that the plethysmography indices give similar information with similar threshold values.

**Table 1**

**Sensibility and specificity: patients are fluid responsive if their values are over the threshold value with a Se and Spe value shown**

| | ΔPPKT | ΔPEPKT | ΔPlethP | ΔPEPPleth |
|---|---|---|---|---|
| Threshold% | 12% | 4% | 12% | 6% |
| Se | 92% | 86% | 88% | 92% |
| Spe | 100% | 100% | 100% | 77% |

**Conclusion** The use of respiratory variation of a digital plethysmography signal (ΔPlethP and ΔPEPPleth) is helpful to assess fluid responsiveness in mechanically ventilated patients.

## P53

### CVP does not reflect changes in preload when optimal PEEP is determined

**I Tóth, T Leiner, A Mikor, T Szakmány, Z Molnár**
*University of Pécs, Hungary*
*Critical Care* 2005, **9(Suppl 1):**P53 (DOI 10.1186/cc3116)

**Objective** High intrathoracic pressures during lung recruitment and defining optimal PEEP may cause haemodynamic instability due decreased venous return [1]. The aim of this study was to evaluate volumetric (ITBV) and pressure (CVP) indicators of preload during the manoeuvre.

**Materials and methods** Eighteen patients suffering from ARDS were recruited. All patients were ventilated in pressure control mode ($FiO_2 = 1.0$, respiratory rate = 20, I:E = 1:1). Following basic haemodynamic measurements and blood gas analysis (Tep) alveolar recruitment was done: PEEP was set at 26 $cmH_2O$, then 40 $cmH_2O$ of pressure amplitude was applied for 40 s (T26). Optimal PEEP was then determined as follows: VT was reduced to 4 ml/kg, then the PEEP was reduced from 26 $cmH_2O$ by 2 $cmH_2O$ every 4 min and the optimal PEEP was defined as 2 $cmH_2O$ above the level of PEEP, where the $PaO_2$ suddenly dropped by >10%. After setting the PEEP at the optimal level, the '40/40' manoeuvre was applied again and the tidal volume was set as 6 ml/kg, end point (Tep). Haemodynamic parameters were determined by arterial thermodilution (PiCCO) during lung recruitment (T26), then every 8 min until the end point was reached (Tep). Data are presented as the mean ± standard deviation. For statistical analysis a paired *t* test and Pearson's correlation was performed.

**Results** The $PaO_2$ improved significantly from T0 to Tep: 203 ± 108 vs 322 ± 101 mmHg, $P < 0.001$. While CI, SVI and ITBVI increased as PEEP was reduced from 26 $cmH_2O$ (T0) to an average of 15 ± 4 $cmH_2O$ (Tep), CVP decreased (Table 1). There was a significant positive correlation between CI and ITBVI ($r = 0.699$, $P < 0.01$), and a significant negative correlation between CI and CVP ($r = -0.294$, $P < 0.05$).

**Table 1**

| | T26 | Tep | *P* |
|---|---|---|---|
| CI (l/min/m²) | 3.6 ± 0.9 | 4.2 ± 1.1 | 0.003 |
| SVI (ml/min/m²) | 32 ± 8 | 36 ± 9 | 0.013 |
| ITBVI (ml/m²) | 794 ± 188 | 870 ± 423 | 0.279 |
| CVP (mmHg) | 24 ± 6 | 19 ± 5 | 0.001 |

**Discussion** As was expected, as PEEP dropped the CI improved due to increased venous return. This increase in preload was reflected by ITBV but not by CVP, which is in accord with findings of a recent animal experiment [2]. These results suggest that CVP cannot be relied on as a measure of preload during lung recruitment or when defining optimal PEEP in ARDS.

**References**

1. Lichtwark-Aschoff M, Zeravik J, Pfeiffer UJ: *Intensive Care Med* 1992, **18:**142-147.
2. Luecke T, Roth H, Herrmann P, *et al.*: *Intensive Care Med* 2004, **30:**119-126.

## P54

### Respiratory variability of aortic blood velocity: predictor of preload responsiveness in healthy spontaneously breathing volunteers

**R Skulec[1], J Belohlavek[1], A Linhart[1], O Cermak[2], T Kovarnik[1], H Skalicka[3], J Kolar[1], M Aschermann[1]**
*[1]2nd Internal Clinic of Cardiology and Angiology, General Faculty Hospital, Prague, Czech Republic; [2]Nemocnice Slany, Czech Republic; [3]Charless University, Prague, Czech Republic*
*Critical Care* 2005, **9(Suppl 1):**P54 (DOI 10.1186/cc3117)

**Introduction** One of the most important problems in therapy of critically ill patients is the assessment of preload responsiveness. Echocardiographic measuring of respiratory variations of aortic blood velocity in ventilated septic shock patients can accurately predict the effect of volume expansion. On the other hand, it remains unclear whether such respiratory variability is a common physiological reaction to hypovolemia and whether its measurement is applicable also in spontaneously breathing patients.

**Aim** To assess whether the respiratory variability of aortic peak blood velocity (ΔVpeak) and the respiratory variability of the aortic velocity time integral measured by continual Doppler (ΔVTI) predict preload responsiveness determined by a more than 15% increase of cardiac index (CI) after volume expansion in spontaneously breathing healthy volunteers.

**Method** ΔVpeak, ΔVTI and CI were measured by transthoracic echocardiography in 20 volunteers at baseline and after

intravenous administration of furosemide (0.5 mg/kg). After diuretic response, volunteers were randomized to rapid intravenous volume expansion (group A) or to a group without volume expansion (group B). With that, the final measurement was performed.
**Results** Hypovolemia induction was associated with a 30% decrease of CI ($P < 0.001$). Correlation between CI decline and a strong increase of ΔVpeak ($r = -0.490$, $P = 0.028$) and ΔVTI ($r = -0.554$, $P = 0.011$) was identified in both groups. In group A, subsequent volume expansion was followed by a drop of ΔVpeak (from 16.04 ± 1.99 to 2.97 ± 1.65, $P < 0.001$) and ΔVTI (from 20.43 ± 5.13 to 3.43 ± 1.68, $P < 0.001$) and an increase of CI in the last measurement strongly correlated with the value of ΔVpeak ($r = 0.782$, $P = 0.008$) and ΔVTI ($r = 0.770$, $P = 0.009$) before volume expansion. Conversely, there was no statistically significant change of ΔVpeak, ΔVTI and CI in group B between the second and the last measurement.
**Conclusions** ΔVpeak and ΔVTI reflect changes of intravascular volume status in healthy spontaneously breathing volunteers, and predict preload responsiveness.

## P55

### Respiratory changes in arterial pulse pressure and fluid responsiveness in spontaneously breathing patients

**S Soubrier[1,2], F Saulnier[1,2], H Hubert[2], P Delour[1], H Lenci[1], T Onimus[1,2], S Nseir[1,2], A Durocher[1,2]**
*[1]CHRU, Lille, France; [2]Lille 2 University, Lille, France*
*Critical Care* 2005, **9(Suppl 1):**P55 (DOI 10.1186/cc3118)

**Introduction** We investigated whether the respiratory changes in arterial pulse pressure (ΔPP), an accurate indicator during mechanical ventilation (MV), and in arterial systolic pressure (ΔPS), easy to calculate, could predict fluid responsiveness in spontaneously breathing patients. The respiratory changes in intrathoracic pressure during spontaneous breathing, reversed compared with MV, could be insufficient to modify loading conditions of ventricles. We thus also tested those indicators during a forced respiratory cycle.
**Methods** We prospectively studied 32 spontaneously breathing ICU patients (mean age: 61 ± 13 years) with clinical signs justifying volume expansion (VE). Hemodynamic measurements were performed during quiet respiration and during a forced respiratory effort (f) at baseline and immediately after a 500 ml 6% hydroxyethylstarch VE. Patients were then separated into responders (R) (increase in stroke volume [SV] assessed by transthoracic echocardiography = 15% after VE) and nonresponders (NR).
**Results** Before VE, ΔPP (13 ± 5% vs 7 ± 3%, $P = 0.003$) and ΔPS (10 ± 4% vs 6 ± 3%, $P = 0.002$) were higher in R ($n = 19$) than in NR ($n = 13$). Receiver operating characteristic (ROC) curve analysis showed that the forced respiratory effort did not sensitize the method (ΔPP f = 0.72 ± 0.09 vs ΔPP = 0.82 ± 0.08, $P = 0.048$ and ΔPS f = 0.69 ± 0.10 vs ΔPS = 0.82 ± 0.08, $P = 0.045$). No statistical difference was observed between ΔPP and ΔPS ROC curves areas (0.81 ± 0.08 vs 0.82 ± 0.08, $P = 0.888$). Using a threshold ΔPP baseline value of 12%, R and NR were discriminated with 93% of specificity and 63% of sensitivity. No relation was observed between ΔPP and ΔPS baseline value and the increase of stoke volume during VE ($r = 0.5$, $P = 0.058$ for ΔPP).
**Conclusion** In spontaneous breathing patients, ΔPP = 12% predicts an increase in SV with high probability (92%) without prejudging the importance of this increase. On the contrary, ΔPP <12% does not allow one to predict fluid responsiveness.

## P56

### A follow-up study of severe sepsis/septic shock patients using echocardiography

**P Marcelino[1,2], N Germano[1], S Heitor[1], L Costa[1], A Fernandes[1], S Marum[1], J Ribeiro[1], M Lopes[2]**
*[1]Hospital Curry Cabral, Lisbon, Portugal; [2]Faculty of Medicine, University of Lisbon, Portugal*
*Critical Care* 2005, **9(Suppl 1):**P56 (DOI 10.1186/cc3119)

**Objective** To follow-up severe sepsis/septic shock patients using echocardiographic parameters.
**Setting and design** A prospective study in a 14-bed medical/surgical ICU.
**Materials and methods** In septic patients the following parameters were obtained: left ventricular (LV) telediastolic dimensions, LV shortening fraction (LVSF), cardiac output (CO) by analysis of pulsed-wave Doppler at the LV outflow tract and inferior vena cava (IVC) evaluation (maximum and minimum dimensions and IVC index). Other parameters were also obtained: age, sex, severity scores (APACHE II, SAPS II, SOFA, and MODS), serum lactate levels, arterial pressure, heart rate, central venous pressure, and need for renal replacement techniques. All data were obtained on the first day of ICU admittance, and at days 2, 3, 5, and then each 5 days. Only patients with three or more evaluations were included. The data analysis was performed by dividing the patients into two groups: survivors (group 1) and nonsurvivors (group 2).
**Results** Twenty-three patients were enrolled. Thirteen patients died (group 2, 56.5%). In group 2 we observed a progressive, but statistically nonsignificant, increase in CO, severity scores, and serum lactate. The IVC index decreased in group 2 over the study time with statistical significance ($P < 0.05$). The main feature of patients in group 1 was a decrease in CO, severity scores and a statistically significant increase in the IVC index. LV dimensions changed in both groups, always not significantly and not linked to a particular outcome or in a consistent manner. Several patients presented with a decrease in LVSF at any time during the study, not linked with any particular outcome, or to changes in CO.
**Conclusion** The fatal course of severe sepsis/septic shock was characterized by a progressive increase in CO, severity scores and serum lactate, although lacking statistical significance. A progressive decrease in the IVC index was statistically significant in the nonsurvivors group. Changes in LV dimension (enlargement) or LVSF were not a constant feature, and we were not able to link these changes to any particular clinical outcome.

## P57

### Assessment of left ventricular diastolic pressure in the emergency room and intensive care unit: a new Doppler index

**M Feissel[1], G Robles[1], O Ruyer[1], J Badie[1], I Mangin[1], J Faller[1], M Slama[2]**
*[1]Centre Hopital Général, Belfort, France; [2]CHU Amiens, France*
*Critical Care* 2005, **9(Suppl 1):**P57 (DOI 10.1186/cc3120)

**Introduction** Assessment of left ventricular diastolic pressure (LVDP) by transthoracic echocardiography (TTE) contributes to the diagnosis of dyspnea in the emergency room and ICU. Classical parameters are derived from mitral blood flow recorded using pulsed Doppler (maximal velocity of early and late mitral wave: E and A), mitral annulus movement using Doppler tissue imaging (early lateral mitral annulus movement: Ea) and early left ventricular inflow propagation velocity (Vp) using M-mode color Doppler. Unfortunately, Doppler tissue imaging and M-mode color Doppler

are not always available on echocardiography machines and these measurements are also time-consuming.

**Objective** In this study, we propose a new simple index obtained exclusively from mitral flow recorded by pulsed Doppler: E/DTE (DTE: deceleration time of E).

**Method** We analysed the sensitivity and specificity of classical indices of LVDP (E/A, E/Ea, E/Vp) and this new index in order to determine their ability to discriminate cardiogenic and noncardiogenic dyspnea.

One hundred and twenty-five patients with acute dyspnea were studied by echocardiography (80 in the emergency room, 45 in the ICU). Cardiogenic dyspnea was defined at hospital discharge on the basis of clinical examination, classical echocardiographic parameters, and clinical course during hospital stay.

**Results** Forty-four percent of patients were considered to have cardiogenic dyspnea and 72% were in sinus rhythm allowing interpretation of the E/A ratio.

Sensitivity and specificity of the parameters analyzed are presented in Table 1 for all patients and for patients in sinus rhythm.

**Table 1**

**Sensitivity and specificity: patients have cardiogenic dyspnea if the values of the different parameters are over the threshold value**

| | E/a threshold 1.5[a] | E/Vp threshold 2[b] | E/Ea threshold 10[b] | E/DTE threshold 0.5[b] |
|---|---|---|---|---|
| Se | 27% | 72% | 75% | 96% |
| Spe | 89% | 90% | 87% | 93% |

[a]For patients in sinus rhythm. [b]For all patients.

**Conclusion** In conclusion, we demonstrated that E/DTE is a very simple, rapidly recorded and highly sensitive and specific index to discriminate cardiogenic and noncardiogenic dyspnea in patients admitted to the emergency room or ICU with normal or altered left ventricular systolic function, whether or not they are in sinus rhythm.

## P58

## Does the central venous pressure still have the authority to evaluate a patient's volume status in clinical routine?

**C Schmidt, W Huber, A Umgelter, R Hollweck, M Mayr, F Geisler, M Retzer-Lidl, M Bajbouj, J Reichenberger, W Reindl, K Stock, K Wagner, S von Delius, R Schmid**

*Second Medical Department, Klinikum Rechts der Isar, Munich, Germany*

*Critical Care* 2005, **9(Suppl 1):**P58 (DOI 10.1186/cc3121)

**Background** Not rarely in clinical routine it is highly difficult to evaluate the volume status of a patient. Therefore, the attending physician can revert to the following parameters in ascending order concerning their invasive character: clinical signs (e.g. inspection of mucosa, skin turgor, the filling of jugular veins, edemas of the lower extremity, auscultation of the lungs), echocardiography, various laboratory findings (e.g. packed cell volume, electrolytes, fractional excretion of sodium), central venous pressure (CVP), thermodilution and pulse contour analysis, respectively, as well as pulmonary arterial wedge pressure.

Recent data suggest that the intrathoracic blood volume index (ITBI) determined by thermodilution can be characterized as the gold standard for the evaluation of a patient's volume status.

However, in clinical routine the CVP, which has been used for decades, is still the most frequently applied nonclinical parameter for volume assessment. However, this is astonishing, because CVP has hardly been tested on modern hemodynamic measurement methods.

**Aim** It was therefore the aim of our prospective study to obtain predictive values for the CVP – for ITBI values in a normal range, as well as for ITBI values falling short of or exceeding the normal range. In other words: Does the CVP still have entitlement or is it more appropriate not to identify any CVP value as to identify one that might be misleading concerning the clinical situation?

**Methods** In 42 patients of an internal ICU, 837 hemodynamic measurements (respectively the average of three single measurements) including CVP as well as ITBI in combination with other thermodilution parameters (such as cardiac output index [CI], stroke volume index [SVI], extravascular lung water index [EVLWI], stroke volume variation) were determined using the PiCCO® system (Pulsion, Munich). Twenty-four of the patients were male, 18 were female; age 60.6 years (± 13.5), APACHE II score of 22.6 on average. Statistics were analysed using SAS version 6.12.

**Results** CVP, 10.9 mmHg (± 5.4); ITBI, 967 ml/m$^2$ (± 170); CI, 4.14 l/m$^2$ (± 1.16); SVI, 1505 dyn s/cm$^5$/m$^2$ (± 514); EVLWI, 9.2 ml/kg (± 4.03).

A total 24.25% of the patients had ITBI $<$ 850, resulting in a positive predictive value (PPV) of CVP of 24.49% and a negative predictive value (NPV) of 75.76% with regard to volume deficit. A total 39.07% of the patients had ITBI $>$ 1000, resulting in a PPV of CVP of 37.74% and a NPV of 59.24% with regard to overfilling. The PPV and NPV for normal ITBI values is 34.80% and 62.16%.

Two hundred and fifteen of 837 (25.70%) measurements were performed under catecholamine therapy; 64 (29.77%) of them were correctly classified with CVP, significantly less than for measurements performed without catecholamine therapy (37.94% accuracy; $P = 0.031$, chi-square test).

**Conclusions** CVP has low PPV and NPV with regard to superior methods of preload assessment such as the ITBI. This low predictive effect is even more pronounced in patients with catecholamine therapy. In summary, volume assessment based only on CVP should be a thing of the past.

## P59

## Are venous pressures obtained from femoral central lines comparable with pressure readings from neck lines?

**V Poulose, S Chuin, A Tee, C Tan**

*Changi General Hospital, Singapore*

*Critical Care* 2005, **9(Suppl 1):**P59 (DOI 10.1186/cc3122)

**Objective** To evaluate whether femoral (femoro-iliac) venous pressures are comparable with the central venous pressures (CVP) obtained from neck lines. We hypothesised that there would not be a clinically significant difference in the readings, in the absence of intra-abdominal hypertension

**Methods** Simultaneous measurements were taken from ICU patients who had both femoral and neck (superior veno-caval) central catheters *in situ*. Only 20 cm femoral lines were considered for the study. Hemodialysis catheters were included in the study. On each occasion, measurements were taken by two independent observers and recorded separately. Intra-abdominal pressures were also measured by the intra-vesical method. We estimated a difference $>$ 2 cm$H_2O$ to be clinically significant

**Results** Thirty sets of readings were taken from 25 patients. Only two sets had a difference $>$ 2 cm. There was no statistically significant difference between the two groups ($P = 0.054$, paired *t* test). The femoro-iliac venous pressures correlated well with the superior vena-caval CVP ($r^2 = 0.721$, $P < 0.01$).

**Conclusions** Venous pressures from femoro-iliac central lines correlated well with CVP taken from neck lines.

**P60**

## The reliability of the central venous pressure measured via catheter inserted in the abdominal vena cava inferior

**M Cengiz, L Dosemeci, M Yilmaz, F Purnek Akin, A Ramazanoglu**
*University of Akdeniz, Antalya, Turkey*
*Critical Care* 2005, **9(Suppl 1):**P60 (DOI 10.1186/cc3123)

**Objective** In our study, we compared the central venous pressure (CVP) measured via catheters inserted in the abdominal vena cava inferior (aVCI) and vena cava superior (VCS) in intensive care patients. The effects of mechanical ventilation, sedation and intra-abdominal pressure (IAP) on CVP at both localisations were evaluated.
**Methods** During a 1-year period, 49 critically ill patients in the ICU were included in the study. In the patients in whom it was decided to change the pre-existing catheter due to prolonged stay, recent catheters were inserted in other localisations from the pre-existing localisations (the recent CVC was inserted in the aVCI if the pre-existing CVC was at the VCS, or the opposite). The pre-existing CVC was kept in place for 24 hours and CVP measurements were performed simultaneously via both of the catheters. IAP was measured via urinary bladder and the sedation scores, ventilation status, sedative drug use, PEEP values, peak and mean airway pressures (PAP and MAP) were recorded during the CVP measurements.
**Results** We performed 148 simultaneous measurements in 49 patients. The mean CVP values obtained from the aVCI and VCS were 7.3 ± 2.9 mmHg and 6.4 ± 3.1 mmHg, respectively ($P < 0.01$). CVP values obtained via the aVCI and VCI were similar in 32.7% of the 123 measurements performed in mechanically ventilated patients. Eight percent of the 25 CVP measurements performed in spontaneously breathing patients were similar ($P < 0.05$). In the CVP measurements performed during IAP < 8 mmHg ($n = 72$) and IAP ≥ 8 mmHg ($n = 76$), the mean differences between aVCI and VCS pressures were 1.04 ± 1.06 mmHg and 1.71 ± 1.4 mmHg, respectively ($P < 0.01$). Mean CVP values obtained from the aVCI were higher when PAP ≥ 25 mmHg or MAP ≥ 12 mmHg ($P < 0.01$). The CVP differences were ≥ 3 mmHg at 26 (17%) of 148 simultaneous measurements.
**Conclusions** We found that mechanical ventilation, PEEP, PAP, MAP and IAP were effective on the difference between CVP values obtained simultaneously via two different routes. Although the mean difference between the pressures obtained via the catheters inserted in the aVCI and VCS (0.9 mmHg) were statistically significant, the clinical importance of this difference may not be important.

**P61**

## Continuous pulse contour analysis after cardiopulmonary bypass in cardiac surgery

**M Sander, C von Heymann, A Foer, A Döpke, W Konertz, C Spies**
*University Hospital Charité, Berlin, Germany*
*Critical Care* 2005, **9(Suppl 1):**P61 (DOI 10.1186/cc3124)

**Introduction** Continous pulse contour analysis is an alternative to the pulmonary artery catheter for continous cardiac index (CI) measurement after cardiac surgery. However, it remains to be determined whether pulse contour analysis has to be re-calibrated after cardiopulmonary bypass (CPB). The aim of the study was to compare continous pulse contour CI analysis after CPB and a period of initial stabilisation with a simultaneous transpulmonary thermodilution measurement of CI.
**Method** After ethical approval and written informed consent 50 patients were included into this prospective study. During aortocoronary bypass surgery, CI was determined by a PiCCO monitor (Pulsion Medical AG, Munich, Germany) in all patients. Prior to surgery the continous pulse contour analysis was calibrated by triple transpulmonary thermodilution measurement of CI. In case of a deviation >10% of a measurement, five measurements were performed and the highest and lowest were rejected. After termination of CPB and initial stabilisation of the patient (20 ± 2 min) continuous pulse contour CI was documented. Simultaneously, the PiCCO monitor was re-calibrated by transpulmonary thermodilution measurement and this CI was documented as well. Statistical analysis was performed by the method described by Bland and Altman.
**Results** After termination of CPB and initial stabilisation of the patient, continous pulse contour analysis determined a CI of 3.1 ± 0.9 l/min/m$^2$. After re-calibration, a CI of 3.6 ± 0.7 l/min/m$^2$ was measured ($P < 0.01$). The mean bias between continous pulse contour analysis CI and transpulmonary thermodilution measurement of CI after CPB was −0.5 l/min/m$^2$. Precision (2SD) was 1.5 l/min/m$^2$.
**Conclusion** Due to the broad distribution and the underestimation of the CI after CPB, a re-calibration of the continous pulse contour analysis is essential after weaning from CPB to prevent false therapeutic consequences.

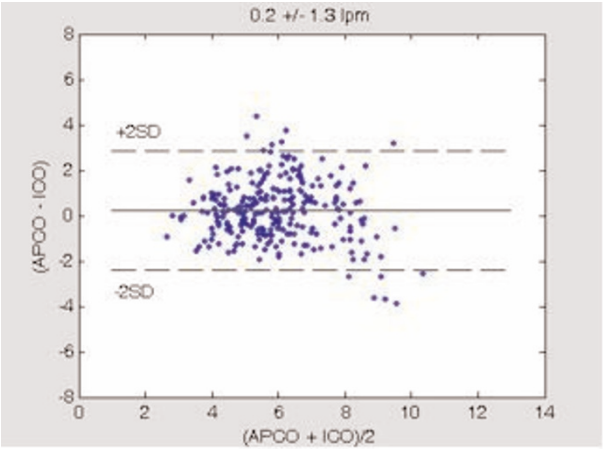
**P62**

## Validation of a continuous cardiac output measurement using arterial pressure waveforms

**W McGee, J Horswell, G Janvier**
*Baystate Medical Center, Springfield, MA, USA; Medical City Dallas Hospital, Dallas, TX, USA; CHU Bordeaux Group Hospitallier Sud, Pessac, France*
*Critical Care* 2005, **9(Suppl 1):**P62 (DOI 10.1186/cc3125)

**Introduction** Intermittent bolus thermodilution cardiac output (ICO) and continuous cardiac output (CCO) measurements with pulmonary artery catheters (PAC) are the most commonly preferred methods of cardiac output (CO) measurement for guiding hemodynamic therapy in the clinical setting. A novel arterial pressure cardiac output (APCO) measurement method requires only access to a radial or femoral artery via a standard arterial catheter and does not require use of venous access or injection of a dilution medium for calibration.
**Hypothesis/methods** We hypothesize that APCO, which measures CO via arterial pressure analysis, is reliable when compared with ICO. We compared a prototype APCO system (FloTrac™; Edwards Lifesciences, Irvine, CA, USA) with PAC (Swan–Ganz®; Edwards Lifesciences, Irvine, CA, USA) routinely used in clinical practice. APCO, ICO, and CCO data were collected from a total of 36 patients (29 cardiac surgery, seven ICU) from three centers (two USA, one France). Average age was 64.1 (± 14.4) years, and 72.2% of the patients were male. Grouped measurements (252 data points) for APCO, ICO and CCO were analyzed for bias, precision and correlation via Bland–Altman analysis.
**Results** Bland–Altman analysis of the differences between CCO and ICO and between APCO and ICO (Fig. 1) were conducted. The analysis yielded a mean bias and precision (± one standard deviation) of 0.8 ± 1.1 and 0.2 ± 1.3 l/min, respectively. APCO trends correlated with ICO in 98% of all data points collected.
**Conclusions** Data show that the APCO method of CCO measurement is reliable and correlates well with ICO measurements when used in critically ill patients. The development

**Figure 1 (abstract P62)**




Bland–Altman analysis of the differences between arterial pressure cardiac output (APCO) and intermittent bolus thermodilution cardiac output (ICO).

of an accurate, less invasive, simple method of measuring CO may contribute to the expansion of CO monitoring to critically ill patients who currently are not monitored with a PAC.

### P63

### The PiCCO system: feasibility and complications of its use in paediatric intensive care

**F Valla, S Lansiaux**
*Hôpital Pédiatrique Debrousse, Lyon, France*
*Critical Care* 2005, **9(Suppl 1):**P63 (DOI 10.1186/cc3126)

**Background and objectives** The PiCCO system provides haemodynamic evaluation and monitoring, using two different techniques: transpulmonar peripheric arterial thermodilution and pulse contour analysis. Paediatric literature is still limited. We retrospectively analysed the use of the PiCCO system in our paediatric intensive care unit, focusing on its feasibility and complications.
**Results** During 16 months, we have used 26 Pulsiocath® (mean patient weight 24 kg and age 80 months) versus 126 arterial catheters (mean patient weight 15 kg and age 40 months).
Complications are presented in Table 1 (major complications include thrombosis, peripheral necrosis and general infection; minor complications include obstruction, temporary ischaemia or oedema and local infection).

**Table 1**

| Complications | Pulsiocath® ($n = 26$) | Arterial catheter ($n = 126$) |
|---|---|---|
| Major | 2 | 2 |
| Minor | 2 | 31 |

**Feasibility** The first values could be measured on average 1 hour after the decision of haemodynamic monitoring had been taken. The use of the PiCCO system failed twice: once the patient died before the first measures, and once because of an arterial stenosis due to a previous catheterization. We encountered technical difficulties with the 3 F Pulsiocath®, because of its weakness.

**Conclusions** The rates of complications are acceptable, in our population characterized by haemodynamic dysfunction and small artery diameters (two parameters known as risk factors for arterial catheterization complication). Its feasibility is good, and technical failure is rare. This technique therefore appears interesting in paediatrics and moderately invasive, compared with other techniques allowing haemodynamic monitoring. It encourages us to extend its use in the paediatric population.

### P64

### Femoral central venous catheter (CVC) versus internal jugular CVC for assessment of haemodynamic parameters by transpulmonary thermodilution using pulse contour cardiac output

**S Grundler, L Macchiavello**
*University Hospital of Wales, Cardiff, UK*
*Critical Care* 2005, **9(Suppl 1):**P64 (DOI 10.1186/cc3127)

**Objective** To compare the intrathoracic blood volume index (ITBVI), cardiac index (CI) and extravascular lung water index (ELWI) values in critically ill patients as measured by transpulmonary thermodilution (TPD) with the pulse contour cardiac output (PiCCO) system, using a femoral central venous catheter (CVC) versus conventional measurement using an internal jugular CVC.
**Introduction** There is no evidence that the use of femoral venous access, instead of internal jugular venous access, for TPD measurements significantly alters the haemodynamic parameters obtained via PiCCO. We postulate that the ITBVI and ELWI differ significantly depending on the CVC site used.
**Design** A prospective, controlled clinical study in an adult critical care unit in a large tertiary-care teaching hospital.
**Patients** Five mechanically ventilated patients with sepsis/septic shock ($n = 4$) and acute liver failure ($n = 1$). Participants had an internal jugular CVC and femoral CVC or triple-lumen vascath in place as part of routine management, as well as a femoral arterial catheter connected to the Pulsion PiCCO system.
**Materials and methods** Haemodynamic parameters were obtained by the TPD technique using bolus injections of 15 ml iced saline solution via the internal jugular and femoral CVCs (order randomly allocated). Bolus injections were performed in $< 8$ s and all measurements were completed in less than 10 min. Where applicable, haemofiltration was discontinued for the duration of the measurements.
**Results** Ten separate sets of paired measurements were obtained from five patients. The paired *t* test (SPSS 11) indicated that the ITBVI was significantly overestimated by an average of 27% ($P < 0.001$) when the femoral CVC was used for the injectate. The CI was not affected by the site of the injectate and, in these preliminary results, there was only marginal overestimation of the ELWI (average 12%, $P = 0.049$) using the femoral CVC.

**Table 1**

| Haemodynamic parameter | Internal jugular central venous catheter | Femoral central venous catheter | % difference | Significance |
|---|---|---|---|---|
| Intrathoracic blood volume index (ml/m$^2$) | 1059 | 1345 | 27 | $< 0.001$ |
| Extravascular lung water index (ml/kg) | 14.2 | 15.8 | 12 | 0.049 |
| Cardiac index (ml/m$^2$) | 4.05 | 4.06 | <1 | 0.92 |

**Conclusions** In critically ill patients the TPD technique with PiCCO using a femoral CVC may not provide as accurate or reliable measures of the ITBVI and possibly the ELWI as conventional measurement with an internal jugular CVC.

## P65

### The effect of continuous veno-venous haemofiltration on PiCCO® haemodynamic parameters

**N Mason, A Froude, B Holst, A Saayman, G Findlay**
*University Hospital of Wales, Cardiff, UK*
*Critical Care* 2005, **9(Suppl 1):**P65 (DOI 10.1186/cc3128)

**Introduction** It is known that measurement of the intrathoracic blood volume (ITBV) is a more accurate estimate of cardiac preload than pressure measurements using central venous or pulmonary artery occlusion pressures. There is evidence to suggest that therapy to reduce extravascular lung water may improve outcome in the critically ill patient. The PiCCO® monitoring system (Pulsion Medical Systems, Munich, Germany) provides an estimate of the ITBV, extravascular lung water (EVLW) and cardiac output (CO) via a thermodilution system. We hypothesised that the use of continuous veno-venous haemofiltration (CVVH) during these measurements could affect the PiCCO® system and give inaccurate results.
**Methods** Twenty-six patients (aged 20–81 years) were studied. Patients were hypotensive, required haemodynamic monitoring and were receiving CVVH for either renal failure or sepsis. Three measurements of CO, ITBV and EVLW were recorded on and off CVVH. The measurements were indexed for body surface area and the mean of each set of three values recorded. Data were normally distributed and analysed by paired *t* tests.
**Results** Results are presented in Table 1 and expressed as the mean and 95% confidence intervals. There was no correlation between CVVH pump speed, fluid exchange rate or use of inotropes and pressors and the changes in cardiovascular parameters on and off CVVH.
**Conclusions** Performing PiCCO® measurements with CVVH running underestimates CO, underestimates ITBV and overestimates EVLW. These measurement errors could result in wrong therapeutic decisions in the management of shocked patients. PiCCO® measurements should be made with CVVH temporarily switched

## P66

### Effects of vasodilation cardiac output measured by PulseCOTM

**K Yamashita[1], T Nishiyama[2], T Yokoyama[1], H Abe[1], M Manabe[1]**
*[1]Kochi Medical School, Kochi, Japan; [2]The University of Tokyo, Japan*
*Critical Care* 2005, **9(Suppl 1):**P66 (DOI 10.1186/cc3129)

**Introduction** PulseCOTM (LiDCO Ltd, London, UK) is a continuous cardiac output (CO) monitor using the pulse-contour method. The pulse-contour method was defined as the method to determine CO from characteristics of the arterial pressure waveform. However, the arterial pressure waveform often changes during surgery because of the arterial compliance changes using vasoactive drugs. These factors may induce miscalculation of the CO by PulseCOTM. In the present study, we investigated the effects of vasodilation induced by prostaglandin $E_1$ ($PGE_1$) on CO measured by PulseCOTM in comparison with CO measured by the bolus thermodilution method.
**Patients and methods** Twelve patients who underwent off-pump coronary artery bypass grafting were enrolled in this study. Patients who suffered from aortic valve stenosis and regurgitation were excluded from the study. After premedication with oral diazepam 10 mg, anesthesia was induced and maintained with midazolam, fentanyl and vecuronium. After induction, radial artery and pulmonary artery catheters (Edwards Lifescience LLC, Irvine, CA, USA) were inserted. The CO and systemic vascular resistance (SVR) were measured after induction to calibrate the PulseCOTM and, subsequently, 10 min after $PGE_1$: (1) 0.01, (2) 0.02 and (3) 0.04 mg/kg/min infusion. CO by the standard thermodilution method was measured using the VigilanceTM system. PulseCOTM was initially calibrated with the value of CO measured by the thermodilution method and no recalibration was performed during the study. For the thermodilution method, the CO was measured three times by injection of 0.2 ml/kg saline of less than 5 degrees and the mean value was calculated.
**Results** Patients were eight males and four females, 68 ± 7 years old, 156 ± 10 cm in height and 61 ± 7 kg in weight. SVR at concentrations (2) and (3) were significantly lower than the control value (Table 1). The correlation coefficient between the two techniques at each point was: (1) $R^2 = 0.71$, (2) $R^2 = 0.18$, (3) $R^2 = 0.41$. The limits of agreement (bias ± two standard deviations of bias) were: (1) 0.04 ± 0.91 l/min, (2) −0.31 ± 1.82 l/min, (3) −0.49 ± 1.33 l/min.
**Conclusions** PulseCOTM might underestimate the CO when the SVR is decreased significantly by infusion of $PGE_1$ 0.02 and 0.04 mg/kg/min in comparison with the CO measured by the bolus thermodilution method.

**Table 1 (abstract P65)**

| | On CVVH | Off CVVH | 95% CI Diff Means | *P* |
|---|---|---|---|---|
| Cardiac index (l/min/m$^2$) | 3.42 (3.10–3.74) | 4.49 (4.08–4.91) | −1.38 to −0.76 | < 0.001 |
| Intrathoracic blood volume index (ml/m$^2$) | 943 (873–1013) | 1324 (1181–1467) | −500 to −262 | < 0.001 |
| Extravascular lung water index (ml/kg) | 11 (9–13) | 9 (7–11) | 1.3–2.8 | < 0.001 |

CVVH, continuous veno-venous haemofiltration; 95% CI Diff Means, 95% confidence interval of difference of means.

**Table 1 (abstract P66)**

| | Control | Prostaglandin $E_1$, 0.01 mg/kg/min | Prostaglandin $E_1$, 0.02 mg/kg/min | Prostaglandin $E_1$, 0.04 mg/kg/min |
|---|---|---|---|---|
| Cardiac output by thermodilution (l/min) | 3.2 ± 0.7 | 3.5 ± 0.9 | 3.9 ± 1.0 | 4.0 ± 0.9 |
| Cardiac output by PulseCOTM (l/min) | 3.2 ± 0.7 | 3.7 ± 0.8 | 3.6 ± 0.7 | 3.5 ± 0.6* |
| Systemic vascular resistance (dyne/s/cm$^5$) | 2099 ± 518 | 1900 ± 528 | 1743 ± 505** | 1604 ± 355** |

*$P < 0.05$ vs thermodilution, **$P < 0.05$ vs control.

**P67**

## USCOM: an accurate system for cardiac output measurement?

**P Lichtenthal[1], R Phillips[2], J Sloniger[1], J Copeland[1]**
*[1]University of Arizona, Tucson, AZ, USA; [2]University of Queensland, Brisbane, Australia*
*Critical Care* 2005, **9(Suppl 1):**P67 (DOI 10.1186/cc3130)

**Introduction** The CardioWest device (Syncardia, Tucson, AZ, USA) is an FDA-approved, total artificial heart system designed to sustain optimized hemodynamics in intractable heart failure patients until suitable organ replacement can be effected. The CardioWest consists of a pneumatic blood pump that delivers accurately measured pulsatile flow to an implanted artificial heart and the native circulation, and displays the delivered hemodynamic parameters. The USCOM device (USCOM Ltd, Sydney, Australia) is a novel non-invasive two-dimensional independent CW Doppler device for assessment of right-sided and left-sided cardiac hemodynamics. This study was to compare and validate the hemodynamic values measured by the USCOM device with those of the controlled CardioWest circulatory model and determine the accuracy of the USCOM device in the clinical setting.
**Methods** Four hundred and sixty serial measurements on four patients were made of right-sided and left-sided cardiac output (CO), stroke volume (SV), and heart rate (HR) using the USCOM device and compared with contemporaneous averaged values recorded on the CardioWest. Flow cross-sectional areas were determined from the CardioWest engineers and used to calculate USCOM flow volumes.
**Results** Mean CO, SV and HR values by USCOM and CardioWest were 7.26 ± 0.66 and 7.23 ± 0.57 l/min, 55.0 ± 4.6 and 54.6 ± 3.7 ml, and 132 ± 5 and 132 ± 4 bpm, respectively. The mean differences between methods for CO, SV, and HR were 0.03 ± 0.49 l/min, 0.42 ± 3.66 ml, and −0.38 ± 3.7 bpm, respectively, with mean errors between measures of 0.34%, 0.64% and −0.38%. See Table 1. There was a good correlation of CO, SV, and HR measures by both methods without significant difference (all $P < 0.005$).

**Table 1**

| Mean values | USCOM | CardioWest |
|---|---|---|
| Cardiac output (l/min) | 7.26 ± 0.66 | 7.23 ± 0.57 |
| Stroke volume (ml) | 55.0 ± 4.6 | 54.6 ± 3.7 |
| Heart rate (bpm) | 132 ± 5 | 132 ± 4 |

**Conclusions** This study confirms both the accuracy of flow measurements using the USCOM device, and the feasibility of obtaining reliable non-invasive cardiac output and other parameters on patients in a clinical setting

**P68**

## Survey of cardiac output monitoring in intensive care units in England and Wales

**B Esdaile[1], R Raobaikady[2]**
*[1]Chelsea & Westminster Hospital, London, UK; [2]St George's Hospital, London, UK*
*Critical Care* 2005, **9(Suppl 1):**P68 (DOI 10.1186/cc3131)

**Background** Haemodynamic monitoring is essential for the management of critically ill patients. There are many methods of monitoring the haemodynamic status of patients, and cardiac output (CO) is one of the major determinants of organ perfusion. Currently there are various techniques available in clinical practice to measure CO in ICUs including pulmonary artery catheter (PAC), oesophageal Doppler, lithium dilution cardiac output (LiDCO) and pulse-induced contour cardiac output (PiCCO) studies. We surveyed current CO monitoring practices in adult ICUs in England and Wales.
**Methods** Adult ICUs in England and Wales were surveyed via telephone. A senior member of the on-call ICU team was consulted to ascertain their unit's preferred CO monitoring techniques.
**Results** Two hundred and twenty-six adult ICUs were surveyed and all the replies were recorded on paper (100% response). In the majority of ICUs, PAC (76%) and oesophageal Doppler (53%) devices are available. Among the other techniques 33% of the ICUs use PiCCO and a further 19% use LiDCO systems for CO monitoring (Table 1). Most of the ICUs (69%) have two or more CO monitoring techniques available and oesophageal Doppler (41%) was preferred as a first choice for CO monitoring. Only 20% of the ICUs regularly measure central venous saturation ($SvO_2$).

**Table 1**

**Cardiac output monitoring technique availability in the ICUs in England and Wales**

| | |
|---|---|
| Pulmonary artery catheters | 76% (171/226) |
| Oesophageal Doppler | 53% (120/226) |
| Lithium dilution cardiac output | 19% (43/226) |
| Pulse-induced contour cardiac output | 33% (74/226) |
| Others | 8% (18/226) |

**Conclusion** The majority of the ICUs have two or more CO monitoring techniques available. The most popular technique for CO monitoring in England and Wales is oesophageal Doppler. This least invasive technique is now the preferred choice of the intensive care physicians in England and Wales. Although PAC is available in most ICUs, only 20% prefer to use them in critically ill patients as the less invasive CO monitoring devices are becoming more accessible.

**P69**

## The use of pulmonary artery catheterization has declined

**S Appavu, J Cowen, M Bunyer**
*University of Illinois College of Medicine, Rockford, IL, USA*
*Critical Care* 2005, **9(Suppl 1):**P69 (DOI 10.1186/cc3132)

**Introduction** Even without the proof of benefit by randomized controlled trials, pulmonary artery catheterization (PAC) has been in wide clinical use in critical care and cardiology since its introduction in 1970. However, during the past decade, several studies and editorials have questioned its safety and have suggested increased risk of morbidity and mortality from its use. During the same period, there were also publications supporting its continued wide use. We hypothesized that these publications had no effect on the frequency of use of the PAC. We performed this study to determine whether or not there was a change in the use of PAC, and if so in which direction and under what circumstances.
**Methods** We studied all the PACs performed during the years 2000 and 2001 in all the hospitals within the state of Illinois, USA. We used the Illinois Health Care Cost Containment Council database for the years of this study. We used the International Classification of Diseases, ninth revision, Clinical Modification (ICD9M) code for PAC to identify all the PACs performed in the

Illinois hospitals during 2000 and 2001. We then analyzed the data based upon age, gender, hospital size, and regions of the state using SPSS statistical software.

**Results** There were 1,636,046 hospital discharges in 2000 and 1,684,089 discharges in 2001 with the PAC rates of 3.65 and 2.98 per 1000 discharges, respectively. In spite of the increase in the number of patients treated in 2001, there was an overall decrease in the use of PAC by 943 (15.8%), from 5965 in 2000 to 5022 in 2001 throughout the state. Among patients older than 75, there was a reduction of 297 (15.5%), from 1917 in 2000 to 1620 in 2001. Among patients 65–74 years of age, there was a reduction of 364 (21%), from 1739 in 2000 to 1375 in 2001. The largest reduction of 57% was seen in the age group of 0–17, from 21 in 2000 to nine in 2001. Among males there was a PAC usage reduction of 522 (15%), from 3492 in 2000 to 2970 in 2001. Among females there was a reduction of 421 (17%), from 2473 in 2000 to 2052 in 2001. Across the state, 10 large medical centers had a 177 (20%) decline in PAC use, from 873 in 2000 to 696 in 2001. All the other hospitals had a 766 (15%) decrease from 5092 to 4326. Among the regions of the state, the city of Chicago, the Rockford area, and the southern region of the state, close to St Louis, had the largest reductions of 431 (39.4%), 199 (40%), and 94 (33.6%), respectively. The central region of the state had a reduction of 15%.

**Conclusion** The use of PAC has decreased on the average of 15% in 1 year. The larger cities and metropolitan areas had a greater decline of 40% in the use of PAC during the same period of time, indicating rapid adaptation of new knowledge.

## P70

### Measurement of rate of pressure development (dP/dtmax) based on femoral artery pressure waveforms: comparison with left ventricular dP/dtmax

**D Robert, S Cromheecke, I Rodrigus, S De Hert**
*University Hospital Antwerp, Edegem, Belgium*
*Critical Care* 2005, **9(Suppl 1):**P70 (DOI 10.1186/cc3133)

**Background** Recently, calculation of the rate of pressure development (dP/dtmax) has been incorporated in the pulse contour cardiac output (PCCO) software technology (Pulsion Medical Systems, Munich, Germany).

Until now its measurement necessitated the presence of an intraventricular pressure catheter. Since dP/dtmax represents a relative load-independent measure of left ventricular function, its availability using standard invasive monitoring technology may provide additional information on the patient's cardiac function. The present study assessed the reliability of PCCO dP/dtmax under different experimental conditions.

**Methods** In 40 coronary surgery patients a high-fidelity pressure catheter was positioned in the left ventricular cavity and a 5-F thermistor-tipped catheter (Pulsiocath PV2015L13) in the femoral artery. Studies were performed before initiation of cardiopulmonary bypass. PCCO dP/dtmax was compared with dP/dtmax measured in the left ventricle under the following experimental conditions: increase in cardiac load obtained by leg elevation, and increase in blood pressure obtained by injection of calcium chloride.

**Results** A weak correlation was observed between absolute dP/dtmax values measured by both systems (leg elevation: $r = 0.36$, $P = 0.001$; calcium: $r = 0.52$, $P < 0.001$) (Bland–Altman bias ± standard deviation: leg elevation: 81 ± 213; calcium: 93 ± 243). However, when changes in dP/dtmax with leg elevation and with calcium administration were analyzed, a close correlation was observed between both measurements (leg elevation: $r = 0.9$, $P < 0.001$; calcium: $r = 0.58$, $P < 0.001$) (Bland–Altman bias + standard deviation: leg elevation: 8 ± 30; calcium: 19± 99).

**Conclusion** The changes in PCCO dP/dtmax with a physiological or pharmacological intervention closely correlated with the changes in left ventricular dP/dtmax. These findings suggest that PCCO dP/dtmax analysis may provide a valuable tool to guide cardiac treatment. Further studies will have to elucidate whether these findings also hold for other interventions.

## P71

### Comparison of non-invasive blood pressure versus radial arterial catheter measurement in an intensive care setting

**R Jackson, M Jonas**
*Southampton University, Southampton, UK*
*Critical Care* 2005, **9(Suppl 1):**P71 (DOI 10.1186/cc3134)

**Introduction** Many critical care patients are haemodynamically unstable and have clinical therapy directed by measurements, such as blood pressure. Surprisingly, there appears a failure to appreciate that indirect devices (non-invasive blood pressure [NIBP]) may be inaccurate in critically ill patients. This is substantiated by several manufacturer's legal disclaimers advising against the use of NIBP devices except in normotensive patients with normal heart rates and rhythms

**Objectives** To evaluate the accuracy of NIBP measurements in the ICU and to investigate sources of error in arterial blood pressure measurements

**Methods** In 47 ICU patients blood pressure was auscultated using a mercury sphygmomanometer and then measured using two NIBP devices (GE Marquette) and Dinamap (Critikon) The arterial line fidelity was validated using a return to flow technique and its harmonic/damping characteristics analysed using a recorded flush test. The non-invasive methods were then compared using standard statistical analysis with the arterial catheter measurements.

**Results** The mercury sphygmomanometer was the most accurate when compared with the arterial line. Both automated devices had unacceptable ranges in the intensive care setting with both algorithms markedly overestimating at low blood pressures. Of the 29 waveforms analysed, 62% of the arterial waveforms had inadequate dynamic responses.

**Figure 1 (abstract P71)**

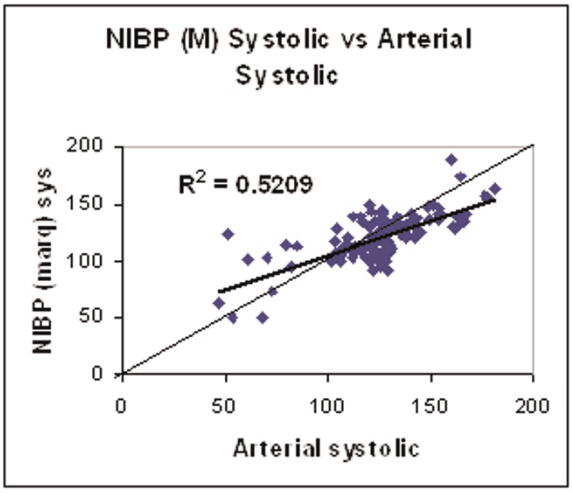


**Figure 2 (abstract P71)**

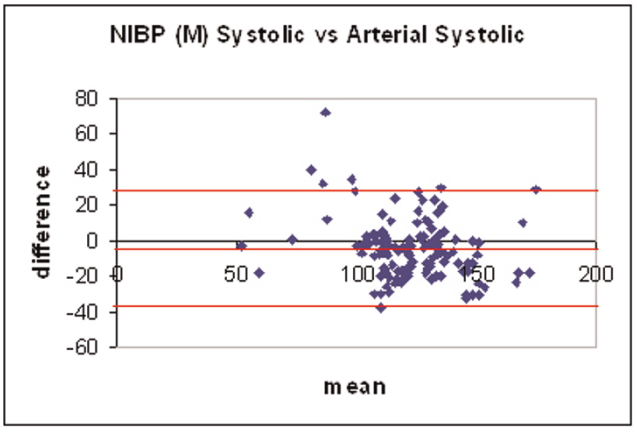
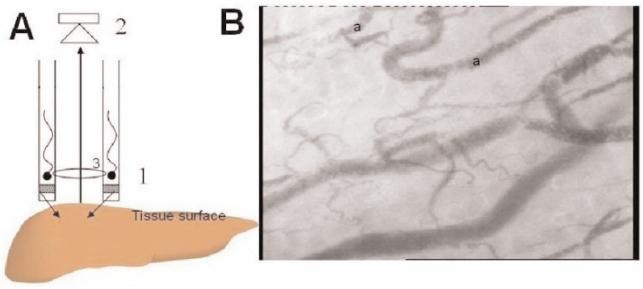



**Figure 1 (abstract P72)**




**(A)** 1, green light-emitting diodes; 2, ccd camera; 3, magnifying lens. **(B)** Sublingual sidestream dark field image showing arterioles (a) in the microcirculation.

**Conclusions** The sphygmomanometer gave acceptable readings versus the arterial catheter. Both NIBP algorithms were inaccurate and unreliable in the intensive care setting, with a tendency to over-read at low arterial pressures and under-read at high arterial pressures. Damping characteristics of the arterial catheters are frequently unfavourable.

## P72

### Sidestream dark field imaging: an improved technique to observe sublingual microcirculation

**C Ince**
*Academic Medical Center, Amsterdam, The Netherlands*
*Critical Care* 2005, **9(Suppl 1):**P72 (DOI 10.1186/cc3135)

Sublingual orthogonal polarization spectral (OPS) imaging has revealed the central role of the microcirculation in the pathophysiology, outcome and treatment of sepsis by its ability to visualize the microcirculation in great detail under clinical conditions. Of particular importance in this context has been the response of the smallest microvessels, the capillaries. OPS imaging illuminates the tissues with polarized green light and measures the reflected light from the tissue surface after filtering out the polarized portion of the reflected light. This filters out the surface reflection of the tissues and allows the visualization of the underlying microcirculation. Due to the reflected and emitted light passing down the same light guide (mainstream), however, OPS imaging is highly sensitive to internal scatter of light. This results in limited visualization of the capillaries due to blurring. The technique also requires high-powered bulky light sources, limiting its utility in difficult conditions such as emergency medicine. In this communication we introduce sidestream dark field (SDF) imaging as a new way of clinical observation of the microcirculation. In this modality a light guide imaging the microcirculation is surrounded by light-emitting diodes (Fig. 1A, 1) of a wavelength (530 nm) absorbed by the hemoglobin of erythrocytes so that they can be clearly observed as flowing cells. Covered by a disposable cap (not shown) the probe is placed on tissue surfaces. The concentrically placed light-emitting diodes at the tip of the probe directly penetrate deep into the tissue illuminating the microcirculation. By not being in direct optical contact with the sensing central core of the probe, no direct surface reflections interfere with the image of the microcirculation. A five or 10 times magnifying lens (Fig. 1A, 3) projects the image onto a video camera (Fig. 1A, 2). This way of observing the microcirculation provides clear images of the capillaries without blurring. The deeper sublingual arterioles can also be clearly observed (Fig. 1B, a). Improved image quality allows better computer automatic analysis of the images and the low energy requirement of SDF imaging further enhances its utility by allowing battery and/or portable computer operation. It is expected that SDF imaging will provide an improved imaging modality of the microcirculation in various clinical scenarios.

**Competing interest** CI is CSO of Micro Vision Medical.

## P73

### Sublingual NIRS and reflectance spectrophotometry: new methods to monitor sublingual oxygen availability

**B Atasever, A van der Veen, P Goedhart, B de Mol, C Ince**
*Academic Medical Center, University of Amsterdam, The Netherlands*
*Critical Care* 2005, **9(Suppl 1):**P73 (DOI 10.1186/cc3136)

**Introduction** Sublingual hemodynamic monitoring (with orthogonal polarization spectral imaging) [1] and metabolic monitoring (with capnography) [2] has revealed detailed information about the microcirculatory and cellular dysfunction in sepsis and shock. These techniques, however, give no information about oxygen availability. To this end we hypothesized that NIRS and reflectance spectrophotometry can be used to monitor sublingual oxygen availability in a non-invasive and continuous manner. We tested this hypothesis in patients during cardiac surgery with cardiopulmonary bypass (CPB) as a clinical environment, where large changes in blood flow and oxygen availability occur.

**Methods** NIRS and reflectance spectrophotometry were used to measure the microcirculatory haemoglobin oxygen saturation and haemoglobin concentration in deeper layers (0–23 mm; InSpectra®; Hutchinson Technology, Arnhem, The Netherlands) and superficial layers (0–8 mm; O2C®; Lea Medizintechnik, Giessen, Germany), respectively. Measurements were made before and just after (<15 min) CPB was initiated.

**Results** Group A (deeper layers, $n = 9$): six males, three females, 72 ± 6 years, BSA 1.83 ± 0.19 $m^2$. Group B (superficial layers, $n = 11$): five males, six females, 70 ± 8 years, BSA 1.81 ± 0.21 $m^2$. The microcirculatory haemoglobin oxygen saturation in group A decreased significantly from 91.9 ± 5.0 to 86.8 ± 6.7% ($P < 0.01$), whereas the microcirculatory haemoglobin oxygen saturation in

group B showed a significant increase from 51.3 ± 4.8 to 62.6 ± 6.8% ($P < 0.01$). In both groups the systemic haemoglobin concentrations decreased significantly after a switch to CPB (from 7.5 ± 1.0 to 5.3 ± 1.1 mmol/l, $P < 0.01$, respectively, from 7.4 ± 1.3 to 4.6 ± 0.9 mmol/l, $P < 0.01$). The sublingual haemoglobin concentrations measured by the different techniques in the different layers showed, however, both a decrease in a similar manner.

**Conclusion** The deeper layers of sublingual tissue monitored by NIRS showed a significant decrease of oxygen availability, whereas the superficial layers showed a significant increase of oxygen availability. It is suggested that redistribution of oxygen availability during CPB can be monitored in this way. It is concluded that monitoring sublingual oxygen availability by these techniques in combination with orthogonal polarization spectral imaging and sublingual capnography will provide comprehensive and integrative information about the functional state of the sublingual microcirculation.

**Acknowledgement** This study is supported by The Netherlands Heart Foundation grant 2001B142.

**References**

1. Spronk PE, Ince C, Gardien MJ, Mathura KR, Oudemans-van Straaten HM, Zandstra DF: **Nitroglycerin in septic shock after intravascular volume resuscitation.** *Lancet* 2002, **360:**1395-1396.
2. Nakagawa Y, Weil MH, Tang W, Sun S, Yamaguchi H, Jin X, Bisera J: **Sublingual capnometry for diagnosis and quantitation of circulatory shock.** *Am J Respir Crit Care Med* 1998, **157:** 1838-1843.

## P74

### Dynamic near-infrared spectroscopy measurements in patients with severe sepsis correlate with invasive hemodynamic measurements

**D Skarda[1], J Taylor[1,2], K Mulier[1], D Myers[3], G Beilman[1]**
*[1]University of Minnesota, Minneapolis, MN, USA; [2]Hennepin County Medical Center, Minneapolis, MN, USA; [3]Hutchinson Technology Inc., Hutchinson, MN USA*
*Critical Care* 2005, **9(Suppl 1):**P74 (DOI 10.1186/cc3137)

**Introduction** Near-infrared spectroscopy (NIRS) has recently been utilized to monitor tissue perfusion in hemorrhagic shock. NIRS has also demonstrated changes in tissue perfusion in severe sepsis. NIRS combined with arterial and venous occlusion cuffing can be used to noninvasively measure thenar and systemic oxygen delivery ($DO_2I$), and oxygen consumption ($VO_2I$). We hypothesized that $DO_2I$ and $VO_2I$ measured by NIRS in patients with severe sepsis will be associated with severity of illness and will correlate with $DO_2I$ and $VO_2I$ measured invasively and by metabolic cart.

**Methods** Septic patients ($n = 10$) were selected for the study who met criteria for severe sepsis, had a pulmonary artery catheter, and had family able to give written consent. Normal age-matched control patients ($n = 9$) were enrolled for comparison. We measured the mean arterial pressure (MAP), serum lactate, plasma hemoglobin, mixed venous oxygen saturation ($SVO_2$), and systemic oxygen consumption via metabolic cart ($metVO_2I$), and calculated systemic oxygen consumption and delivery via pulmonary artery catheter ($paVO_2I$, $paDO_2I$), thenar oxygen delivery ($nir.thenarDO_2I$), thenar oxygen consumption ($nir.thenarVO_2I$), systemic oxygen delivery ($nir.sysDO_2I$), systemic oxygen consumption ($nir.sysVO_2I$), and mixed venous oxygen saturation ($nirSVO_2$) in patients with severe sepsis in a surgical ICU. The same data, without invasive hemodynamic measurements, were measured once in volunteers. NIRS data were collected from the thenar eminence using the Inspectra system (Hutchinson Technology, Hutchinson, MN, USA). A poor outcome was defined by multiorgan dysfunction 7 days after the development of severe sepsis, death within 28 days of severe sepsis, or both.

**Results** Healthy volunteers and septic patients were similar with respect to age and sex. MAP and hemoglobin were decreased and serum lactate increased in septic patients compared with healthy volunteers. In septic patients, $nirSVO_2$ correlated with $SVO_2$ ($P < 0.001$), $nir.sysVO_2I$ correlated with $metVO_2I$ ($P = 0.017$), and $nir.sysDO_2I$ correlated with $paDO_2I$ ($P < 0.001$). Interestingly, $paVO_2I$ did not correlate well with $metVO_2I$ ($P = 0.435$). Of these patients, 4/10 developed poor outcome. Patients with poor outcomes had significant elevations of $paDO_2I$ ($P < 0.001$), $nir.thenarDO_2I$ ($P = 0.005$), $nir.sysDO_2I$ ($P < 0.001$), and $SVO_2$ ($P < 0.001$) compared with patients who did not develop poor outcomes.

**Conclusions** NIRS measurements of $SVO_2$ and $DO_2I$ correlated with invasively measured values in patients with severe sepsis. Interestingly, $nir.sysVO_2I$ correlated more closely to $metVO_2I$ than did $paVO_2I$. Dynamic NIRS values were predictive of outcomes. This suggests a role for NIRS measurements of $SVO_2$, $DO_2I$, and $VO_2I$ in patients in severe sepsis.

## P75

### Impact of early sepsis on oxygen delivery in the microvasculature

**G Fraser[1], D Goldman[2], M Sharpe[1], C Ellis[1]**
*[1]University of Western Ontario, London, ON, Canada; [2]New Jersey Institute of Technology, Newark, NJ, USA*
*Critical Care* 2005, **9(Suppl 1):**P75 (DOI 10.1186/cc3138)

A defining characteristic of sepsis is progressive blood flow dysfunction in the microvasculature of organs remote to the original site of injury. Previous work has established that microvascular oxygen transport is compromised in sepsis due to a loss of perfused capillaries. In a companion study to this project, which investigated the role of leukocyte traffic in sepsis, it was observed that increased transit times of leukocytes passing through the capillary bed not only resulted in the occlusion of some capillaries, but also served to cause some vessels to experience prolonged periods of low flow. The objective of the present study was to examine how the progressive loss of functional capillary density (FCD) impacts oxygen transport and consumption in skeletal muscle during sepsis. Hemodynamic and oxygen saturation data from video recordings are incorporated into an experiment-based mathematical model of oxygen transport in a three-dimensional volume. This modeling helps to further our understanding of the impact that capillary loss has on tissue oxygenation and consumption. Sepsis was induced in rats by cecal ligation and perforation (CLP). Rats received crystalloid fluid resuscitation to maintain blood pressure and hematocrit at baseline levels. Microvascular flow was observed in the extensor digitorum muscle using a dual wavelength intravital video microscopy set-up. The same field of view was recorded at 30 min intervals between 2 and 5 hours post CLP to follow the progression of capillary dysfunction. Individual capillaries were analyzed for oxygen saturations and hemodynamics. As sepsis progresses we observed that capillaries' hemodynamic profiles transiently change between normal, stopped and fast flow states. Although it has previously been assumed that once a capillary becomes occluded flow is not easily re-established, we observed that capillaries could suddenly become reperfused after being occluded for up to 1 hour or more. The occlusion of capillaries was found to decrease oxygen saturations in nearby vessels by as much as 20%. Subsequent recruitment of previously unperfused capillaries was shown to

increase saturations in adjacent vessels by as much as 50%. Changes in perfusion of adjacent vessels had a greater impact on oxygen saturation than changes in hematocrit or velocity in the vessel itself. At 2, 3 and 4 hours post CLP the percentage of stopped flow vessels was 17%, 28% and 48% in CLP compared with 13%, 13% and 20% in sham. The extent of FCD loss is progressive over the course of the injury. However, it is important to note that while the percentage of occluded capillaries increases, the individual vessels constituting this percentage were variable. Our study suggests that in this early stage where the FCD is in transition, affected tissue experiences dynamic changes in tissue oxygenation. This highlights the importance of understanding the mechanisms responsible for this dynamic change in FCD.

## P76

### Increased leukocyte transit times through capillaries contributes to maldistribution of flow

**T Jeganathan[1], G Fraser[1], D Goldman[2], M Sharpe[1], CG Ellis[1]**
*[1]University of Western Ontario, London, ON, Canada; [2]New Jersey Institute of Technology, Newark, NJ, USA*
*Critical Care* 2005, **9(Suppl 1):**P76 (DOI 10.1186/cc3139)

Sepsis has been shown to result in a decrease in functional capillary density (FCD) in animal models and in septic patients. We have previously shown that increased numbers of stopped flow capillaries result in a fall in capillary oxygen saturation [1,2]. The goal of this study was to determine whether leukocytes played a role in capillary occlusion. Our objective was to examine leukocyte traffic within the microcirculation in the extensor digitorum longus (EDL) muscle using fluorescently (rhodamine 6G) labeled leukocytes and to correlate this with the loss of FCD seen in a 5 hour rat cecal ligation and perforation (CLP) model of sepsis. Ten rats were randomized to sham ($n = 5$) or CLP ($n = 5$). The capillary bed in the EDL muscle was observed using intravital video microscopy. Functional capillary density was determined prior to the loss of FCD at 1.5 hours after induction of sepsis or the sham procedure. The location of all capillaries within a single capillary network from arteriole to venule was mapped. At 4 hours rhodamine 6G was injected and the same capillary network was observed using fluorescence microscopy to determine which capillaries contained flowing or stopped leukocytes and to measure leukocyte transit times. Leukocytes were found to preferentially traverse a subpopulation of capillaries in both sham (40% of total capillary paths) and CLP animals (60%). In the sham animals, 80% of the leukocytes traversed the capillary bed in $<1$ s and only 7±4% of all capillaries had stopped flowing by 5 hours. In CLP animals, leukocyte transit times increased significantly with only 15% traversing in $<1$ s and 40% taking longer than 10 s (of which half remained stopped for $> 30$ s). In CLP animals 45 ± 5% of capillaries had stopped flowing by 5 hours; 63 ± 2% of these capillaries were preferential flow paths for leukocytes. The slowing of leukocytes through the capillary bed suggested the possible role of selectins. Six CLP animals were treated with fucoidin, a nonselective general inhibitor of selectins. Fucoidin prevented the increase in leukocyte transit times and the loss of FCD at 5 hours, indicating that selectins were involved in the slowing of leukocytes in sepsis. Leukocytes play a significant role in the maldistribution of capillary blood flow through the loss of perfused capillaries and increased leukocyte transit times. Both effects probably cause a concomitant fall in oxygen saturation in neighboring capillaries, leading to periods of tissue hypoxia.

**Acknowledgement** This research was funded by a grant from the Canadian Institutes for Health Research to CGE.

### References

1. Ellis CG, Bateman RM, Sharpe MD, Sibbald WJ, Gill R: **Effect of a maldistribution of microvascular blood flow on capillary O(2) extraction in sepsis.** *Am J Physiol Heart Circ Physiol* 2002, **282:**H156-H164.
2. Goldman D, Bateman RM, Ellis CG: **Effect of sepsis on skeletal muscle oxygen consumption and tissue oxygenation: interpreting capillary oxygen transport data using a mathematical model.** *Am J Physiol Heart Circ Physiol* 2004, **287:**H2535-H2544.

## P77

### Activated protein C improves intestinal microcirculation in experimental endotoxemia in the rat

**A Knöck, S Diedrich, D Pavlovic, M Wendt, C Lehmann**
*Greifswald University, Greifswald, Germany*
*Critical Care* 2005, **9(Suppl 1):**P77 (DOI 10.1186/cc3140)

**Objective** We studied the effects of activated protein C (APC) on the intestinal microcirculation during experimental endotoxemia in rats using intravital microscopy.
**Design** A prospective, randomized, controlled animal study.
**Setting** Experimental laboratory of a university.
**Animals** Forty-four male Lewis rats.
**Interventions** The animals were divided into four groups. Group 1 served as control. Group 2 (lipopolysaccharide *Escherichia coli* [LPS]) and group 3 (LPS + APC) received endotoxin infusion (15 mg/kg). In groups 3 and 4 (APC) 2 mg/kg Drotrecogin alfa (activated) was administered. All animals underwent studies of intestinal functional capillary density (FCD) and leukocyte adherence on venular endothelium in the microcirculation of the terminal ileum by intravital fluorescence microscopy (IVM).
**Measurements and results** APC reduced significantly the number of firmly adhering leukocytes in V3 venules (416.5 ± 54.7) and V1 venules (235.4 ± 59.8) (Fig. 1) as compared with LPS (678.9 ± 144.4 in V3 venules; 374.5 ± 90.4 in V1 venules; Fig. 2). The FCD (cm/cm$^2$) in the mucosa of LPS rats receiving APC was increased (172.2 ± 14.1) as compared with the LPS rats (143.1 ± 9.6, $P < 0.05$). The FCD of longitudinal and circular muscular layers showed a better perfusion in rats treated with APC (172.2 ± 14.1 vs 167.4 ± 16.7) in comparison with untreated animals (143.1 ± 9.6 vs 141.1 ± 15.2, $P < 0.05$).

**Figure 1 (abstract P77)**

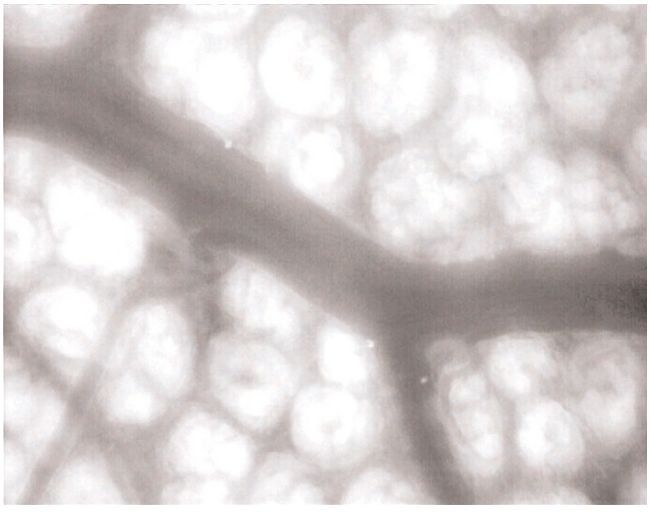


**Figure 2 (abstract P77)**

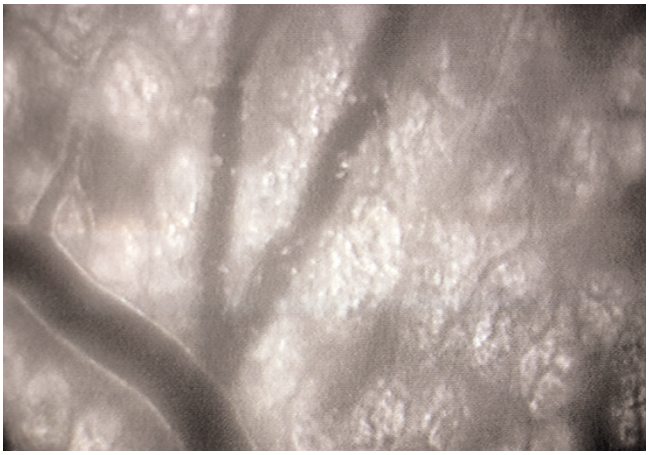
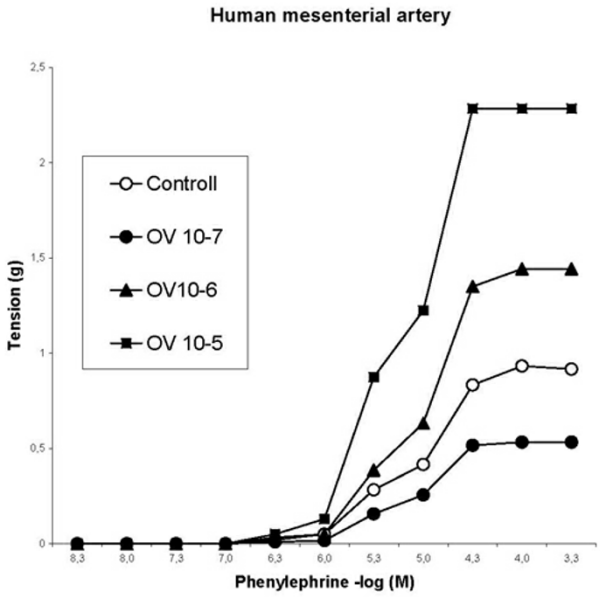


**Figure 1 (abstract P78)**




**Conclusion** APC administration in endotoxemic animals improved microcirculatory perfusion. Moreover, APC treatment revealed anti-inflammatory effects by reducing leukocyte adherence to the endothelium.

**P78**

## Reversal of lipopolysaccharide-induced hyporeactivity in rat aorta and human mesenteric artery *in vitro* by orthovanadate

**H Erber, C Lehmann, M Gruendling, T Wenzel, A Stier, M Wendt, D Pavlovic**
*Greifswald University, Greifswald, Germany*
*Critical Care* 2005, **9(Suppl 1):**P78 (DOI 10.1186/cc3141)

**Background** Endotoxemia is characterised by vascular hyporeactivity (VHR) that is partially caused by the excess of nitric oxide (NO) production. The agent that affects $Ca^{2+}$ transport or the $Ca^{2+}$ sensitivity of contraction may theoretically reverse VHR.
**Methods** The VHR was induced *in vitro* by incubating (for 6 hours) rat aortal rings, with or without endothelium (± ENDO), or human mesenteric arterial rings (HMA) endothelium intact (+ENDO), with lipopolysaccharide *Escherichia coli* (LPS) ($10^{-3}$ g/l). In addition, the preparations (12 groups, $n = 7$ each) were preincubation (10 min) with various concentrations of sodium-orthovanadate (OV) ($10^{-7}$, $10^{-6}$, or $10^{-5}$ M) and then the contractile response to phenylephrine (PE) was examined *in vitro*.
**Results** We found that the presence of endothelium diminished sensitivity to PE in rat aorta (+ENDO, EC50: 5.88 ± 0.11 vs –ENDO, EC50: 6.84 ± 0.15, respectively), a result probably of an overproduction of nitric oxide and potassium channel activation. The preincubation with OV had no effect on sensitivity to PE in rat aorta (± ENDO) and HMA (+ENDO) as compared with corresponding controls (without OV [–OV]). However, preincubation with OV increased maximal tension (Tmax) to PE, as compared with the control (–OV). Tmax (kg/g, dry muscle), control versus OV (concentration): rat aorta (–ENDO): 0.87 ± 0.19 vs 1.42 ± 0.23 ($10^{-7}$ M), 1.56 ± 0.28 ($10^{-6}$ M) and 2.33 ± 0.69 ($10^{-5}$ M); rat aorta (+ENDO): 0.88 ± 0.21 vs 1.53 ± 0.35 ($10^{-7}$ M), 1.35 ± 0.30 ($10^{-6}$ M) and 2.55 ± 0.68 ($10^{-5}$ M); and human mesenteric artery (+ENDO): 1.12 ± 0.23 vs 0.37 ± 0.14 ($10^{-7}$ M), 2.06 ± 0.21 ($10^{-6}$ M) and 3.00 ± 0.07 ($10^{-5}$ M), respectively.
**Conclusion** These findings demonstrated that the VHR in rat aorta and human mesenteric artery could be reversed by an inhibition of calcium removal and/or inhibition of tyrosine phosphatase activity. It should be verified whether in human preparations taken from septic patients orthovanadate could have some beneficial effects on vascular hyporeactivity.

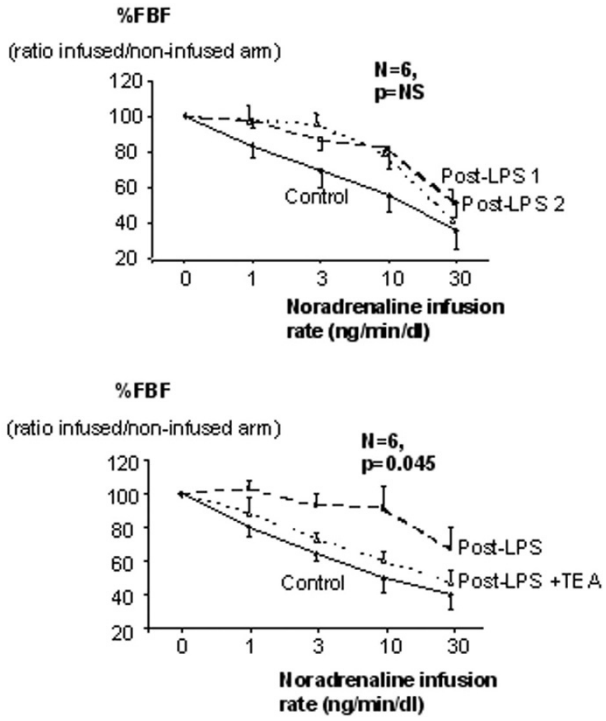
**P79**

## Potassium channel blockade restores the attenuated noradrenaline sensitivity in human endotoxemia

**P Pickkers, M Dorresteijn, P Smits, H Van der Hoeven**
*Radboud University Nijmegen Medical Centre, The Netherlands*
*Critical Care* 2005, **9(Suppl 1):**P79 (DOI 10.1186/cc3142)

**Introduction** Vasodilatory shock is a major problem in intensive care medicine. It is recently recognized that activation of vascular potassium (K) channels may play an important role in sepsis-induced vasodilation and attenuated sensitivity to noradrenaline. Pharmacological K-channel blockade restores blood pressure and improves mortality in animal models of sepsis. Human data are lacking. We examined whether endotoxin administration to healthy volunteers resulted in an attenuated noradrenaline sensitivity and whether this effect could be restored by the K-channel blocker tetra-ethyl ammonium (TEA).
**Methods** Human volunteers received 2 ng/kg *Escherichia coli* endotoxin. The brachial artery was cannulated for infusion of drugs. Forearm blood flow (FBF) was measured using venous occlusion plethysmography. Noradrenaline was administrated intra-arterially at 1, 3, 10, 30 ng/min/dl and the vasoconstrictive response to noradrenaline was determined before endotoxin was administrated. Four hours after endotoxin administration the noradrenaline dose–response curve was repeated to determine the effects of endotoxin. One hour later the K-channel blocker TEA was administrated intra-arterially (1 mg/min/dl), after which the noradrenaline dose response curve was determined again. During the experiments continuous monitoring of heart rate and mean arterial pressure was performed and blood samples were taken to determine effects on standard laboratory values. Data are expressed as mean ±

**Figure 1 (abstract P79)**




standard error of the mean. Differences were tested by analysis of variance repeated measures or Student *t* test, as appropriate. $P < 0.05$ was considered to indicate significance.

**Results** Endotoxin administration induced the expected flu-like symptoms and fever (maximum temperature 38.3 ± 0.1°C, $P < 0.001$). Mean arterial pressure decreased from 93 ± 2 to 79 ± 2 mmHg ($P < 0.001$) and the heart rate increased from 60 ± 2 to 95 ± 2 bpm ($P < 0.001$). After the administration of endotoxin, leucocytes increased to 14.2 ± 0.6 × $10^9$/l ($P < 0.001$) and C-reactive protein increased to 36.0 ± 2.7 mg/l ($P < 0.001$). Intra-arterial noradrenaline infusion decreased forearm blood flow: percentage of baseline ratio (infused/noninfused arm), 100 ± 0%, 84 ± 4%, 70 ± 4%, 55 ± 4%, 38 ± 4%. Following endotoxin administration, the noradrenaline-induced vasoconstriction was attenuated: 100 ± 0%, 101 ± 4%, 92 ± 4%, 83 ± 6%, 56 ± 7% ($P < 0.001$, pooled data, $n = 25$). Time control experiments ($n = 6$) demonstrated excellent repeatability of the attenuated noradrenaline response after the administration of endotoxin (see Fig. 1, top). Intra-arterial infusion of the K-channel blocker TEA almost completely restored the vasoconstrictive effect of noradrenaline (see Fig. 1, bottom; $n = 6$, $P = 0.045$).

**Conclusions** In experimental human endotoxemia, noradrenaline sensitivity is decreased. K-channel blocker TEA almost completely restores the vasoconstrictive effects of noradrenaline. Our study demonstrates that endotoxin-induced vascular K-channel activation plays a major role in the observed attenuated sensitivity to noradrenaline during human endotoxemia.

## P80

### Dose-dependent and temporal effects of pentoxifylline in a rat model of acute hepatic failure

**T Rahman[1], H Hodgson[2]**
*[1]St George's Hospital, London, UK; [2]Royal Free Campus, University College, London, UK*
*Critical Care* 2005, **9(Suppl 1):**P80 (DOI 10.1186/cc3143)

**Introduction** The methylxanthine pentoxifylline (PTX) is known to increase intracellular cAMP concentrations by inhibiting phospodiesterases. Despite beneficial *in vitro* effects its role in acute hepatic failure (AHF) is controversial. Several studies have demonstrated no benefit in the use of PTX in AHF, sepsis or shock.
**Aims** To investigate three hypotheses: (1) the use of PTX leads to improved outcome in AHF; (2) this effect is dose dependent; and (3) improved outcome is limited by temporal constraints. We will compare PTX administration pre and post hepatic injury.
**Methods** We have previously described a robust and reproducible model of AHF in the Wistar rat. The animals were randomly allocated into five groups (each $n = 10$): Group I received 2 × intra-peritoneal injections of thioacetamide (TAA) 8 hours apart (500 mg/kg). Groups II and III were pretreatment groups: Group II was pretreated with low-dose PTX (25 mg/kg body weight) and Group III was pretreated with high-dose PTX (300 mg/kg) and received the TAA protocol as in Group I. Groups IV and V were post-treatment groups. All followed the protocol for Group I; however, 30 min prior to receiving the second dose of TAA they received low-dose PTX (Group IV) and high-dose PTX (Group V). Clinical, biochemical and pathological analysis occurred at 24-hour time points.
**Results** Encephalopathy, blood ammonia levels and transaminitis is significantly reduced by pretreatment with low-dose PTX (Group II) ($P < 0.05$). A significant reduction in mortality is seen in Group II where mortality at 96 hours is 30% compared with greater than 90% in the other pretreatment group ($P < 0.005$) and 70% in the TAA-treated animals ($P < 0.005$). This reduction in clinical and biochemical parameters is not seen in the post-treated groups.
**Conclusion** Low-dose pretreatment with PTX significantly improves encehalopathy, biochemical markers of AHF and mortality compared with controls (TAA only). Beneficial effects are, however, negated if PTX is administered at high dose pretreatment or any dose post-treatment with TAA, exacerbating hepatic injury, increasing mortality and therefore demonstrating dose-dependent and temporal constraints.

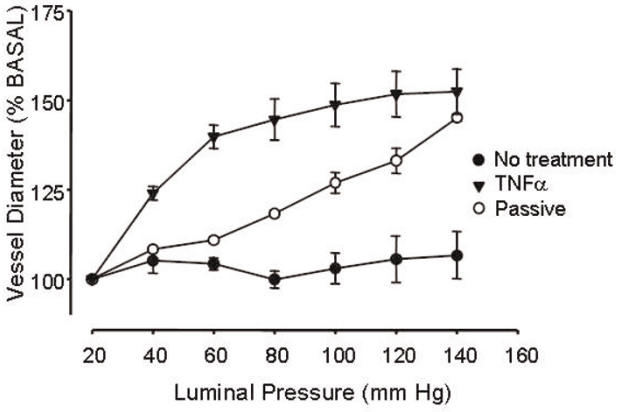
## P81

### Tumor necrosis factor increases the sensitivity of the contractile apparatus in isolated mouse resistance arteries via a calcium-dependent mechanism

**Y Ouellette**
*Mayo Clinic College of Medicine, Rochester, MN, USA*
*Critical Care* 2005, **9(Suppl 1):**P81 (DOI 10.1186/cc3144)

**Introduction** The myogenic response is the modulation of resistance artery diameter in response to changes in luminal pressure. It is thought to be an important determinant of peripheral vascular resistance and therefore of arterial blood pressure. Since altered peripheral resistance is known to occur during the systemic inflammatory response syndrome (such as in sepsis), we suspect that an abnormal myogenic response might be responsible. Our main objective is to assess the effects of tumor necrosis factor alpha (TNF-$\alpha$) on the myogenic response of mouse mesenteric resistance arteries and to determine the role of $Ca^{2+}$ in this response.

**Figure 1 (abstract P81)**




**Hypothesis** TNF-α reduces the myogenic response in mesenteric resistance arteries by reducing smooth muscle cell $Ca^{2+}$ sensitivity.
**Methods and results** Vessels (external diameter ~150–200 μm) were mounted on a pressure myograph and allowed to develop myogenic constriction. After endothelial cell removal, baseline measurements were obtained and measurements were repeated 1 hour after treatment with TNF-α (50 ng/ml). TNF-α resulted in reduced myogenic tone at increasing luminal pressures (see Fig. 1). To determine the role of $Ca^{2+}$ in this response, the passive internal diameter was measured in a $Ca^{2+}$-free solution. TNF-α significantly shifted the $Ca^{2+}$–diameter relation to the right, as assessed by stepwise increasing of extracellular $Ca^{2+}$ (0–1.5 mmol/l) in depolarized skeletal muscle resistance arteries. This suggests a decreased $Ca^{2+}$ sensitization of the smooth muscle cell contractile apparatus.
**Conclusion** We conclude that, in mouse mesenteric resistance arteries, TNF-α treatment results in reduced myogenic tone that may be due partly to decreased $Ca^{2+}$ sensitivity. These results suggests that the microvascular dysfunction seen during sepsis could be due in part to a decreased myogenic response.

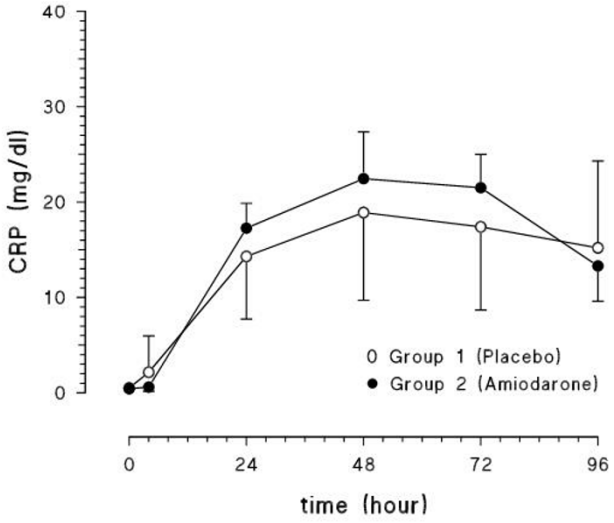
### P82

### Influence of amiodarone treatment on inflammation during cardiopulmonary bypass

**G Delle Karth, A Buberl, B Meyer, G Zorn, J Wojta, G Wollenek, M Grimm, M Hiesmayer, A Lassnig, G Heinz**
*Medical University of Vienna, Austria*
*Critical Care* 2005, **9(Suppl 1):**P82 (DOI 10.1186/cc3145)

**Introduction** Cardiopulmonary bypass (CPB) induces a systemic inflammatory response (SIRS), which causes significant morbidity or even mortality. Amiodarone (Amio) has shown to reduce postoperative atrial fibrillation and also to reduce tumor necrosis factor alpha (TNF-α) production *in vitro*. Whether Amio reduces the post CPB SIRS is unknown
**Hypothesis** The present study sought to investigate the anti-inflammatory properties of Amio after CABG using CPB.
**Methods** Twenty-two patients undergoing elective CABG were randomly assigned to receive 600 mg Amio orally 7 days pre surgery daily and 45 mg/hour intravenously for 48 hours after initiation of CPB (10 patients, group 2) or placebo (12 patients, group 1). Two patients in group 2 were excluded due to withdrawn consent during the loading phase. The primary endpoint was the

**Figure 1 (abstract P82)**




C-reactive protein (CRP) curve (AUC) up to 96 hours, and secondary endpoints were fibrinogen and WBC up to 96 hours and TNF-α and IL-6 curves up to 48 hours post surgery, respectively.
**Results** Baseline characteristics were not different between groups (age 61 ± 8 vs 62 ± 10 years, male 7/8 vs 10/12, EF 576 vs 53 ± 7%, SAPS II score 19 ± 3 vs 21 ± 8, CPB duration 78 ± 15 vs 79 ± 17 min, group 2 vs group 1, $P$ = not significant). Amio did not reduce the postoperative CRP AUC when compared with placebo (1579 ± 260 vs 1397 ± 617, $P$ = 0.44; Fig. 1). Furthermore, no significant differences in the AUCs of fibrinogen, WBC, TNF-α and IL-6 were observed. Length of ICU and hospital stay were not different between groups (2.4 ± 1.5 vs 2.7 ± 2.0 days, $P$ = not significant and 9.0 ± 1.4 and 13.3 ± 7.1 days, $P$ = not significant, group 2 vs group 1, respectively). There were no deaths in either group.
**Conclusions** In this pilot study, there was no difference in the post CPB inflammatory reaction between Amio-treated and placebo-treated patients.

### P83

### Effects of sarpogrelate, a 5-hydroxytriptamine 2A receptor antagonist on endotoxin shock in rats

**T Nishiyama**
*The University of Tokyo, Saitama, Japan*
*Critical Care* 2005, **9(Suppl 1):**P83 (DOI 10.1186/cc3146)

**Introduction** It is known that 5-hydroxytriptamine (5-HT)2A receptors have some roles in vascular constriction, platelet aggregation, and superoxide production by neutrophils. 5-HT2A receptor antagonists are therefore expected to be effective for sepsis. The present study was performed to investigate the effects of sarpogrelate, a 5-HT2A receptor antagonist on endotoxin shock in rats.
**Methods** Male Sprague–Dawley rats were anesthetized with halothane. Catheters were inserted into the femoral artery and the femoral vein. Sarpogrelate 0, 3, or 10 mg/kg dissolved in 0.5 ml clear water was administered intravenously followed by 10 mg/kg endotoxin 5 min later. The blood pressure (BP), pulse rate (PR), and survival rate were monitored for 4 hours in 20 rats at each

dose. Arterial blood was drawn before, 2 and 4 hours after endotoxin administration to measure IL-1β, IL-6, IL-8, IL-10, and tumor necrosis factor alpha (TNF-α) (another eight rats at each dose).

**Results** The decreases in BP and PR were significantly bigger in the 0 mg/kg group than the 3 mg/kg and 10 mg/kg groups. Survival rates were significantly lower in the 0 mg/kg group than the other two groups. IL-1β at 4 hours was significantly higher in the 0 mg/kg group than the other two groups. TNF-α at 2 hours was significantly lower in the 3 mg/kg group than the other two groups. The data at 4 hours are presented in Table 1 as the mean ± standard deviation.

**Table 1**

| | 0 mg/kg | 3 mg/kg | 10 mg/kg |
|---|---|---|---|
| Blood pressure (mmHg) | 45 ± 26 | 90 ± 18* | 80 ± 21* |
| Pulse rate (beats/min) | 105 ± 35 | 285 ± 25* | 278 ± 29* |
| Survival rate | 3/20 | 18/20* | 15/20* |
| IL-1β (pg/ml) | 244 ± 56 | 85 ± 33* | 53 ± 15* |
| IL-6 (ng/ml) | 6.8 ± 1.7 | 5.4 ± 1.8 | 7.1 ± 2.9 |
| IL-8 (ng/ml) | 46.0 ± 16.7 | 35.4 ± 9.7 | 38.4 ± 10.1 |
| IL-10 (pg/ml) | 844 ± 384 | 1047 ± 520 | 1163 ± 315 |
| Tumor necrosis factor α (ng/ml) | 2.2 ± 0.5 | 2.0 ± 0.9 | 2.1 ± 0.6 |

*$P < 0.05$ vs 0 mg/kg.

**Discussion** Pretreatment with sarpogrelate inhibited the decrease in BP and PR and decreased mortality. Cytokine levels had big variations, but sarpogrelate had a tendency to decrease IL-1β, IL-6, IL-8, and TNF-α, and to increase IL-10. Sarpogrelate 3 mg/kg was more effective than 10 mg/kg; probably 10 mg/kg decreased BP more than 3 mg/kg. In the preliminary study, BP was dose-dependently decreased by sarpogrelate and 30 mg/kg killed animals. Therefore, sarpogrelate 3 mg/kg might be the choice.

**Conclusion** Intravenous sarpogrelate might be effective for endotoxin shock.

## P84

### Possible involvement of rho kinase 1 (rock 1) in cecal ligation and puncture-induced sepsis

**I Cinel, M Ark, H Kubat, T Karabacak, H Serinol, L Tamer, U Oral**
*Mersin University School of Medicine, Mersin, Turkey*
*Critical Care* 2005, **9(Suppl 1):**P84 (DOI 10.1186/cc3147)

We have previously demonstrated that following cecal ligation and puncture (CLP) there is an increase in lung epithelial apoptosis in a rat model [1]. On the other hand, it has been shown that the rho/rho kinase pathway is involved in mechanisms of several aspects such as endothelial cell dysfunction and apoptosis. However, the role of rho kinase in the concept of sepsis-induced apoptosis has yet to be elucidated. In this study, to investigate the possible contribution of rho/rho kinase signalling in CLP-induced lung injury, rho kinase expression and the possible protective effect of the administration of an inhibitor of rho kinase, (+)-(R)-trans-4-1-aminoethyl-*N*-4-pyridyl cyclohexanecarboxamide dihydrochloride monohydrate (Y-27632), has been investigated in rats in this model.

Thirty-two male Wistar rats were randomly divided into four groups: (1) sham, (2) CLP, (3) sham + Y27632, (4) CLP + Y27632. Y27632 was administered at 1.5 mg/kg, intaperitoneally, 20 min before performing operations. Twenty-four hours later, histopathology and apoptosis were assessed by H&E and immunohistochemically by caspase-3 to demonstrate septic lung injury. Additionally, expression of rock 1 and rock 2 proteins in lung tissue was analyzed by western blotting, and the contribution of oxidative damage was assessed by measuring the levels of thiobarbituric acid reactive substances (TBARS) and the 3-L-nitrotirozin (3-NT)/total tyrosine ratio.

The TBARS and 3-NT/total tirosine ratio levels in lung homogenates were found to be increased (11.05 ± 0.31 vs 29.855 ± 2.87) (0.1485 ± 0.10 vs 0.281 ± 0.05) in the CLP group compared with the sham group, and the administration of Y27632 prevented their increase (8.86 ± 1.87) (0.178 ± 0.02) significantly ($P < 0.05$). The number of apoptotic cells was significantly lower in the CLP + Y27632 group than CLP group and this finding was supported by caspase-3 expression in the lung. Lung histopathology was also protected by Y27632 in CLP-induced sepsis. Immunoblot experiments revealed the increased expression of active fragment of rock 1 in the CLP group. However, rock 2 expressions were similar in all groups.

In conclusion, since CLP induced active fragmentation of rock 1 and rho-kinase inhibitor prevented peroxynitrite-mediated apoptotic lung injury in this CLP-induced sepsis model, this suggests that rho-kinase plays an important role in apoptotic lung injury. Our data indicate that rock 1 or downstream components of this pathway may be potential targets for the development of novel therapies in sepsis.

**Reference**

1. Ozdülger A, Cinel I, Koksel O, *et al.*: **The protective effect of N-acetylcysteine on apoptotic lung injury in cecal ligation and puncture-induced sepsis model.** *Shock* 2003, **19:**366-372.

## P85

### Peri-mortem and ante-mortem haemodynamic profile of severe sepsis/septic shock

**P Marcelino[1,2], N Germano[1], A Fernandes[1], S Marum[1], J Ribeiro[1], M Lopes[2]**
*[1]Hospital Curry Cabral, Lisbon, Portugal; [2]Faculty of Medicine, University of Lisbon, Portugal*
*Critical Care* 2005, **9(Suppl 1):**P85 (DOI 10.1186/cc3148)

**Objective** To describe the main haemodynamic parameters obtained in patients with severe sepsis and septic shock, who died several hours later.

**Design** A prospective, observational study, using transthoracic echocardiography.

**Setting** A medical/surgical 14-bed ICU.

**Materials and methods** In the patients enrolled the following echocardiographic parameters were obtained: left ventricular (LV) telediastolic dimension, left ventricular shortening fraction (LVSF), cardiac output (CO), by determination of the flow velocity integral of the LV out-flow tract using pulsed-wave Doppler analysis, and the determination of the inferior vena cava (IVC) maximal and minimum dimensions, and the IVC index (maximum dimension – minimum dimension × 100/maximum dimension). A CO between 2.4 l/min/m$^2$ and 4 l/min/m$^2$ was considered normal, as well as a LVSF of 36 ± 6%. Based on the characteristics of CO and the IVC index, we considered the following types of shock and/or hypotension: cardiogenic (low CO and IVC index < 25%), vasogenic (normal or high CO and variable IVC index), and hypovolemic (low CO and IVC index > 50%).

Twenty-seven patients were enrolled, and divided into two groups: group 1 consisted of patients with a haemodynamic evaluation up to 6 hours before death (peri-mortem group, $n = 14$), and group 2 with a haemodynamic evaluation between 6 and 12 hours before death (ante-mortem group, $n = 13$). In all patients was determined: age, sex, arterial pressure, heart rate, APACHE II score, SAPS II, SOFA, MODS, serum lactate, and central venous pressure (CVP).

**Results** Six patients in group 1 and three patients in group 2 presented a situation compatible with a cardiogenic type of

hypotension. The remainder presented as a vasogenic type of hypotension. Eight patients in group 1 presented LVSF < 30%, as well as four patients in group 2 All severity scores of group 1 were slightly higher, as well as serum lactate levels. The main results are presented in Table 1, with means and standard deviation for each variable.

**Table 1**

| Parameter | Group 1 | Group 2 |
|---|---|---|
| APACHE II score | 40 ± 4 | 39 ± 9 |
| SAPS II | 95 ± 8 | 88 ± 9 |
| SOFA | 18.7 ± 1.7 | 16 ± 4 |
| MODS | 17.3 ± 2 | 15 ± 3.6 |
| Serum lactate | 11.7 ± 5.7 | 9.8 ± 5.6 |
| Cardiac output (l/min/m$^2$) | 3692 ± 1254 | 2829 ± 958 |
| Left ventricular shortening fraction (%) | 32 ± 5.6 | 28.4 ± 7.3 |

**Conclusions** Septic shock presents as a vasogenic type until the late disease course. A LV failure with a cardiogenic type of situation characterizes better the later stages, up to 6 hours before death occurs.

## P86

### Effect of reduced bronchial circulation on the lung fluid flux in the case of combined burn and smoke inhalation injury in sheep

**N Morita, P Enkhbaatar, F Schmalstieg, M Westphal, M Maybauer, D Maybauer, L Traber, D Traber**
*UTMB, Galveston, TX, USA*
*Critical Care* 2005, **9(Suppl 1):**P86 (DOI 10.1186/cc3149)

**Introduction** We reported that the bronchial circulation contributes to pulmonary function after acute lung injury with smoke inhalation. But the observation period was 24 hours. We hypothesize that the bronchial circulation plays a major role in the lung injury seen with the combination of burn and smoke inhalation injury.
**Method** Merino ewes ($n = 13$) were surgically prepared for chronic study. After a recovery (5–7 days) they were randomly divided into three groups: (1) the bronchial artery was ligated ($n = 5$); (2) sham group ($n = 5$), the bronchial artery was surgically exposed but left intact without ligation; (3) the bronchial artery was exposed, not ligated and the animals were not injured. One day after these operations, under deep halothane anesthesia, two groups received a tracheotomy and were subjected to a 40% third-degree flame burn and insufflated with 48 breaths of cotton smoke inhalation or were sham injured. All sheep were mechanically ventilated and resuscitated by Ringer's lactate for 48 hours. We confirmed the ligation of the bronchial artery with microspheres. Statistics were performed using repeated-measures analysis of variance for repeated measurements and Scheffe's post hoc comparisons was used and $P < 0.05$ was considered significant. Data are expressed as mean ± standard error of the mean.
**Result** After ligation (24 hours), blood flow of the bronchi decreased to 24.48% of the baseline value. Pulmonary dysfunction after the combined injury in the ligation group was significantly reduced. Lung lymph flow, an index of pulmonary transvascular fluid flux, was markedly increased in in the ligated and intact groups. Ligation reduced this response (24 hours: sham 65 ± 5.0; ligation 15.5 ± 7.51; sham–sham 9.4 ± 5.6; 48 hours: sham 64.5 ± 16.5; ligation 12.58 ± 5.743; sham–sham 7.25 ± 3.95 ml/hour). Ligation also improved the $PaO_2/FiO_2$ ratio (24 hours: sham 270 ± 99.347; ligation 390.381 ± 53.781; sham–sham 595 ± 13.856; 48 hours: sham 132.5 ± 33.15; ligation 375 ± 62.253; sham–sham 592.33 ± 8.95). PMN production also decreased (24 hours: sham 32.5 ± 31.8; ligation 6.2 ± 2.2; 48 hours: sham 38.3 ± 46.2; ligation 2.7 ± 2.6 × $10^6$).
**Conclusions** Bronchial circulation plays a significant role in the lung inflammation after combined burn and smoke inhalation injury.
**Acknowledgements** Supported by National Institutes of Health GM066312, Shriners of N America 8450 and 8954.

## P87

### A pilot study of left main bronchus pulse oximetry

**XR Wang, YJ Zheng, J Tian, ZH Wang, ZY Pan**
*Department of Anesthesiology, Renji Hospital, Shanghai Second Medical University, Shanghai, China*
*Critical Care* 2005, **9(Suppl 1):**P87 (DOI 10.1186/cc3150)

**Objective** To assess the feasibility and accuracy of measuring mixed venous oxygen saturation ($SvO_2$) through the left main bronchus ($SpO_2$trathea). The hypothesis that tracheal oximetry readings are not primarily derived from the tracheal mucosa was also tested. The pulmonary artery lies in close proximity to the bronchus, with nothing but some connective tissues in the interval, raising the possibility that an appropriately located and directed bronchial oximetry probe might be able to derive oximetry readings from the mixed venous system. The present study was undertaken to test the feasibility of measuring $SvO_2$ through the left main bronchus ($SpO_2$trachea), and to compare $SpO_2$trachea with the Swan–Ganz catheter $SpO_2$ ($SvO_2$catheter) and oxygen saturation from pulmonary artery samples ($SvO_2$blood) in hemodynamically stable, well-oxygenated, anesthetized white swines. We also tested the hypothesis that bronchial oximetry readings are primarily derived from the pulmonary artery, not the tracheal mucosa. Furthermore, the stability and accuracy of $SpO_2$trachea was tested by correlating the oximetry readings with altered $SvO_2$ or with internal environment instability.
**Methods** Twenty hemodynamically stable, well-oxygenated, anesthetized white swine were studied. A Robertshaw double-lumen tracheal tube was directed toward the left main bronchus using a fibrobronchoscope. A single-use pediatric pulse oximeter was attached to the left lateral surface of the tube. $SpO_2$trathea, Swan–Ganz catheter $SpO_2$ ($SvO_2$catheter) and oxygen saturation from pulmonary artery samples ($SvO_2$blood) were taken with the intracuff pressure at 0–60 $cmH_2O$. The intracuff pressure was then set at 60 $cmH_2O$, and changes of $SvO_2$ were induced using three different concentrations of inspiratory oxygen. The influence of the changes on $SpO_2$trathea, $SvO_2$catheter and $SvO_2$blood was measured respectively at the same time.
**Results** $SpO_2$trathea was the same as $SvO_2$catheter and $SvO_2$blood at an intracuff pressure of 10–60 $cmH_2O$, but was less when the intracuff pressure was zero ($P < 0.001$ compared with $SvO_2$catheter or $SvO_2$blood) in hemodynamically stable states. The descending of $SvO_2$ followed with decreased inspiratory oxygen concentration. $SpO_2$trachea agreed with $SvO_2$catheter and $SvO_2$blood at each concentration with significant correlation among them.
**Conclusion** Left main bronchus $SpO_2$ is feasible and provides similar readings to $SvO_2$catheter and $SvO_2$blood in hemodynamically stable or low saturation states. Tracheal oximetry readings are not primarily derived from the tracheal mucosa. The technique merits further evaluation.

**P88**

## Relationship between extravascular lung water and oxygenation indices in patients with acute respiratory failure

**J Graf, V Tomicic, P Aguilera, M Espinoza, C Canals**
*Clinica Alemana de Santiago, Chile*
*Critical Care* 2005, **9(Suppl 1):**P88 (DOI 10.1186/cc3151)

**Introduction** The main strategy to restore organ perfusion in critically ill patients is fluid administration, which increases the likelihood of acquiring pulmonary edema with detrimental effects on gas exchange. The thermal-dye dilution technique has been used to measure extravascular lung water (EVLW). Recently, this technique has been simplified using only the thermal indicator [1]. The relationship between EVLW and the $PaO_2/FiO_2$ ratio has been sparsely studied and described as weak [2]. Oxygenation index (OI) relates $PaO_2$, $FiO_2$, and mean airway pressure (Paw) by the following formula: OI = Paw × $FiO_2$ × 100 / $PaO_2$ [3]. We are not aware of publications correlating EVLW with OI.
**Methods** Simultaneous measurements of EVLW, arterial blood gases and Paw were performed in mechanically ventilated patients at different moments of their illness course. EVLW was measured by a single transpulmonary thermodilution technique using a PiCCO® monitor. The EVLW value was indexed (EVLWi) by the predicted body weight [4]. $PaO_2/FiO_2$ and OI were calculated and correlated with EVLWi using linear regression analysis with a 95% confidence interval (CI).
**Results** We studied 21 patients, 20 with ALI/ARDS (age 64 ± 19 years, APACHE II score 24.4 ± 6.8, SOFA 10.3 ± 3.2, LIS 2.55 ± 0.57). Mean admission EVLWi, Paw, $PaO_2/FiO_2$ and OI values were 14 ± 6.5 ml/kg, 17.8 ± 3.9 $cmH_2O$, 186 ± 80 and 12.1 ±7.5, respectively. We obtained 152 EVLWi measurements with simultaneous $PaO_2/FiO_2$ and OI values. A significant negative correlation was found between EVLWi and $PaO_2/FiO_2$ ($r = -0.53$, CI −0.63 to −0.40, $P < 0.01$) (Fig. 1). A significant positive correlation was found between EVLWi and OI ($r = 0.70$, CI 0.60–0.77, $P < 0.01$) (Fig. 2).
**Conclusions** There is a stronger correlation between EVLWi and OI than with $PaO_2/FiO_2$. This finding emphasizes the importance of incorporating Paw into the evaluation of patient oxygenation during mechanical ventilation.

**Figure 1 (abstract P88)**

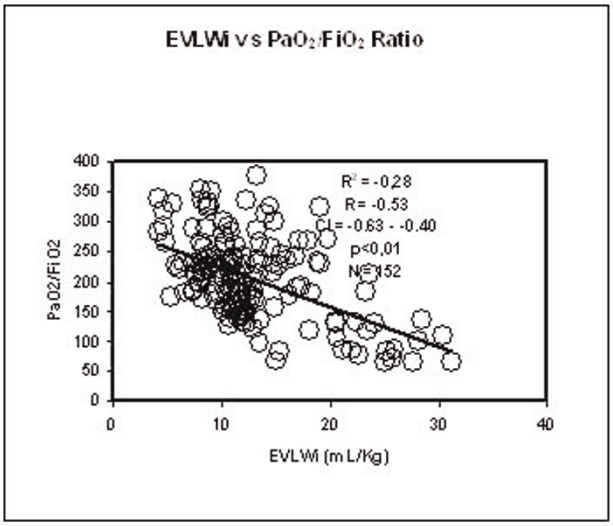
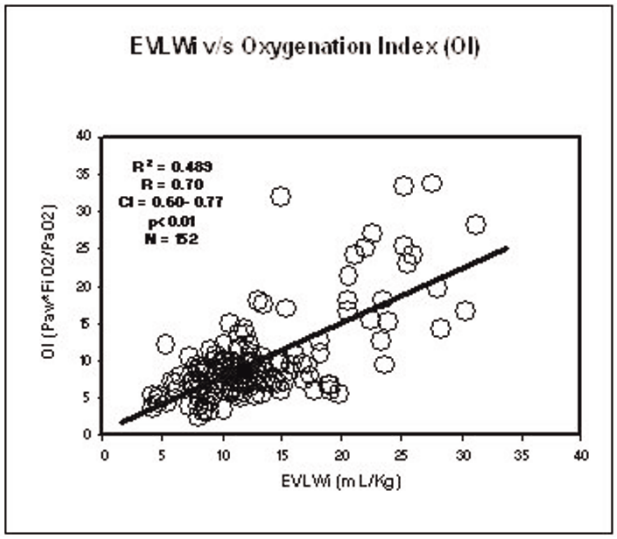



**Figure 2 (abstract P88)**




**References**
1. *Intensive Care Med* 2000, **26:**180-187.
2. *Chest* 2004, **125:**1166.
3. *J Pediatr* 1985, **106:**963-969.
4. *N Engl J Med* 2000, **342:**1301-1308.

**P89**

## Diagnostic test of the desaturation index and the calculated desaturation index to identify acute lung injury and/or acute respiratory distress syndrome at the bedside

**G Vazquez de Anda[1,2], J Arzate Villafaña[1,2], J Talavera Piña[2], S Laraza[1], J Gutierrez[1], D Rodriguez Cadena[2]**
*[1]ISSEMYM Medical Center, Toluca, Mexico; [2]Universidad Autonoma del Estado de Mexico, Toluca, Mexico*
*Critical Care* 2005, **9(Suppl 1):**P89 (DOI 10.1186/cc3152)

**Introduction** We have previously shown that the desaturation index (DI) and the calculated desaturation index (Dic) have a statistical correlation with several indices of gas exchange and with lung infiltrates on the thorax X-ray. However, the utility of the DI and Dic as a diagnostic tool has never been tested. The aim of this study is therefore to determine the capability of the DI and the DIc: to identify acute lung injury (ALI) and/or acute respiratory distress syndrome (ARDS) at the bedside.
**Patients and methods** Patients with and without ALI and/or acute respiratory failure (ARDS) were followed during the period of mechanical ventilation. Every morning, blood gases analysis and thorax X-rays were taken and definitions for ALI/ARDS were completed according to the American–European Consensus Conference. We registered the positive end expiratory pressure, inspired fraction of oxygen ($FiO_2$) and arterial saturation by pulse oximetry ($SpO_2$) to calculate the Dic. Then, in order to determine the DI, all patients were subjected to breathe 100% oxygen, with a gradual reduction of the $FiO_2$ to 21%, in steps of 20% lasting 8 min each, and at each step the $SpO_2$ was registered (we stop the maneover after reaching 85% of the $SpO_2$). Finally, we calculated the DI according our equation that has been described previously. Two or more quadrants with infiltrates on the thorax X-ray and $PaO_2/FiO_2$ ratio (adjusted to high altitude) lower than 221

mmHg were considered positive for ALI/ARDS. The sensitivity and specificity were calculated according to conventional equations.
**Results** During the study period, 198 ALI/ARDS definitions were completed. Table 1 presents the sensitivity and specificity tests for the DI and the Dic. Results are shown as the percentage and confidence interval

**Table 1**

| | $Pao_2/FiO_2$ | Thorax X-ray | ALI/ARDS |
|---|---|---|---|
| DI sensitivity | 0.86 (0.78–0.91) | 0.77 (0.69–0.84) | 0.87 (0.78–0.92) |
| DI specificity | 0.84 (0.75–0.89) | 0.85 (0.76–0.91) | 0.83 (0.74–0.87) |
| DIc sensitivity | 0.93 (0.87–0.97) | 0.85 (0.77–0.90) | 0.99 (0.95–1) |
| DIc specificity | 0.82 (0.74–0.89) | 0.85 (0.76–0.91) | 0.93 (0.86–0.97) |

ALI, acute lung injury; ARDS, acute respiratory distress syndrome; DI, desaturation index; Dic, calculated desaturation index.

**Conclusion** We conclude that the DI and the DIC, which are non-invasive indices, have an acceptable sensitivity and specificity to identify ALI/ARDS patients at the bedside.

## P90

## Effect of pharmacological inhibition of chloride transport on lung fluid balance in acute *Escherichia coli* pneumonia in mice

**L Robriquet[1], Y Song[2], H Folkesson[3], J Frank[2], A Verkman[4], M Matthay[2]**
*[1]CHRU, Lille, France; [2]Cardiovascular Research Institute, San Francisco, CA, USA; [3]Department of Physiology, Rootstown, OH, USA; [4]Department of Medicine and Department of Physiology, Cardiovascular Research Institute, San Francisco, CA, USA*
*Critical Care* 2005, **9(Suppl 1):**P90 (DOI 10.1186/cc3153)

**Introduction** Clearance of fluid from the alveolar spaces primary depends on the active sodium transport across distal lung epithelium. Some experimental studies supported a potential role for the cystic fibrosis transmembrane conductance regulator (CFTR), especially in the cAMP-mediated upregulation of fluid clearance. Hypothetically, pharmacological inhibition of $Cl^-$ channels could worsen lung edema by decreasing the clearance of alveolar edema. In this study, we tested the affect of chloride transport inhibition on lung edema formation in acute pneumonia.
**Methods** A mouse model of acute pneumonia was established using IT instillation of *Escherichia coli* (107 cfu). Basal and isoproterenol (0.1 mM)-stimulated alveolar fluid clearance were studied using the *in situ* mice model. Glibenclamide (0.1 mM) or a specific CFTR-inhibitor (100 mM CFTR-172) was instilled into the lung to study the effects of CFTR blockade.
**Results** In response to cAMP stimulation by isoproterenol, clearance was inhibited by glibenclamide or the CFTR-172 inhibitor (respectively, 12.2 ± 0.39% and 9.7 ± 3.5% versus 20.7 ± 2.9% in the control group, $P < 0.05$). Four hours after bacterial instillation, the lung wet-to-dry ratio and lung vascular permeability as measured by the extravascular accumulation of $^{125}$I-albumin were increased compared with the control group (respectively, 4.8 ± 0.18 g/g versus 3.8 ± 0.18 g/g, $P < 0.05$ and 61.8 ± 10.4 µl versus 20 ± 5.9 µl, $P < 0.05$). No significant statistical change was found among lung water and endothelial permeability in the glibenclamide or CFTR-172 inhibitor group.
**Conclusion** These experiments indicated that the c-AMP-dependent fluid clearance from the distal airspaces of the lung involves chloride transport by CFTR. *In vivo*, we found no change in pulmonary edema formation following *E. coli* intratracheal instillation. These data suggest that chloride transport is not a major mechanism in lung edema formation in a mouse model of acute pneumonia.

## P91

## Effect of beta-adrenergic agonist on alveolar fluid clearance in rats with acute lung injury

**H Qiu, H Sun, Y Yang**
*Nanjing Zhong-Da Hospital, Southeast University, Nanjing, China*
*Critical Care* 2005, **9(Suppl 1):**P91 (DOI 10.1186/cc3154)

**Background** Although it is well known that beta-adrenergic agonist improves alveolar fluid clearance (AFC) in several animal species, it is not known whether beta-adrenergic agonist improves AFC in infectious acute lung injury (ALI). This study is aimed at investigating the effect of beta-adrenergic agonist (dobutamine) on AFC in rats with infectious ALI and exploring the associated mechanism.
**Methods** Thirty-two male Sprague–Dawley rats were randomly divided into four groups (normal control group, ALI group, dobutamine control group, dobutamine treatment group). A rat with ALI was induced by infusion of endotoxin intravenously. Alveolar fluid clearance was measured by the single-nuclide tracer technique. α-Rat epithelial sodium channel (α-rENaC), β-rENaC and γ-rENaC mRNA expressions were measured by RT-PCR.
**Results** AFC of the ALI group was 14.0 ± 1.2%, which was significantly lower than the normal control group (21.0 ± 3.9%), the dobutamine treatment group (20.0 ± 3.8%) and the dobutamine control group (26.6 ± 1.6%) ($P < 0.05$). AFC of the dobutamine control group was significantly higher than the normal control group, dobutamine treatment group and ALI group ($P < 0.05$). α-rENaC and β-rENaC mRNA expressions of the ALI group (1.4 ± 0.4 and 0.7 ± 0.8, respectively) and the dobutamine treatment group (1.38 ± 0.13 and 0.71 ± 0.17, respectively) were significantly higher than the dobutamine control group (1.01 ± 0.14 and 0.58 ± 0.12, respectively) and the normal control group (1.00 ± 0.28 and 0.44 ± 0.11, respectively) ($P < 0.05$). There were no significant differences of α-rENaC and β-rENaC mRNA expressions between the normal control group and dobutamine control group, and no significant difference between the ALI group and dobutamine treatment group ($P > 0.05$). γ-rENaC mRNA expressions of the dobutamine control group and dobutamine treatment group were 0.90 ± 0.19 and 0.97 ± 0.15, respectively, which were significantly higher than normal control group (0.69 ± 0.10) and the ALI group (0.7 ± 0.3) ($P < 0.05$). There was no significant difference of γ-rENaC mRNA expressions between the normal control group and the ALI group, and no significant difference between the dobutamine control group and the dobutamine treatment group ($P > 0.05$).
**Conclusion** Beta-adrenergic agonist may upregulate γ-rENaC expression and improve AFC in rats with endotoxin-induced ALI. It may be beneficial to increase AFC and reduce lung edema using beta-adrenergic agonist in ALI patients.

## P92

## Effect of beta-adrenergic agonist on alveolar fluid clearance in rats

**H Qiu, Y Yang, H Sun**
*Nanjing Zhong-Da Hospital, Southeast University, Nanjing, China*
*Critical Care* 2005, **9(Suppl 1):**P92 (DOI 10.1186/cc3155)

**Objective** To investigate the effect and the associated mechanism of beta-adrenergic agonist on alveolar fluid clearance (AFC) in rats.
**Methods** Forty-eight Sprague–Dawley male rats were randomly divided into six groups (normal control group, dobutamine group,

amiloride [specific inhibitor of epithelial sodium channel] group, dobutamine + amiloride group, dobutamine + atenolol [specific beta-1 antagonist] group, dobutamine + ICI118,551 [specific beta-2 antagonist] group). AFC was measured by the single-nuclide tracer technique. Alpha-rat epithelial sodium channel (alpha-rENaC), beta-rENaC and gamma-rENaC mRNA expressions were measured by RT-PCR.

**Results** (1) AFC of the dobutamine group and dobutamine + atenolol group were 26.6 ± 1.6% and 25.0 ± 5.3%, respectively, which were significantly higher than the normal control group (21.0 ± 3.9%) and dobutamine + ICI 118,551 group (21.0 ± 4.8%) ($P < 0.05$). There was no significant difference of AFC between the dobutamine group and dobutamine + atenolol group ($P > 0.05$); and no significant difference of AFC between the normal control group and dobutamine + ICI 118,551 group ($P > 0.05$). (2) AFC of the amiloride group was 6.0 ± 2.8%, which was significantly lower than the normal control group ($P < 0.05$). (3) AFC of the dobutamine + amiloride group was 10.0 ± 2.3%, significantly higher than the amiloride group ($P < 0.05$). (4) Gamma-rENaC mRNA expression of the dobutamine group and dobutamine + atenolol group was 0.90 ± 0.19 and 0.90 ± 0.09, respectively, significantly higher than the normal control group (0.69 ± 0.09) and dobutamine + ICI 118,551 group (0.68 ± 0.06) ($P < 0.05$). There was no significant difference of gamma-rENaC mRNA expression between the dobutamine group and dobutamine + atenolol group; and no significant difference of gamma-rENaC mRNA expression between the normal control group and dobutamine + ICI 118,551 group ($P < 0.05$). There was no significant difference of alpha-rENaC and beta-rENaC mRNA expressions between each group ($P > 0.05$). (5) Gamma-rENaC mRNA expression of the dobutamine + amiloride group was 0.70 ± 0.14, significantly lower than the dobutamine group and dobutamine + atenolol group ($P < 0.05$).

**Conclusion** The amiloride-sensitive NaC pathway was important for lung epithelium to actively transport alveolar fluid. The effect of beta-2 adrenergic stimulation may upregulate gamma-rENaC expression and also stimulate the amiloride-insensitive NaC pathway to improve AFC in rats.

### P93

### Change of extravascular lung water in sheep with early acute respiratory distress syndrome

**H Qiu, H Sun**
*Nanjing Zhong-Da Hospital, Southeast University, Nanjing, China*
*Critical Care* 2005, **9(Suppl 1):**P93 (DOI 10.1186/cc3156)

**Objective** To determine the change of extravascular lung water (EVLW) and the effect of positive end-expiratory pressure (PEEP) and cardiac output (CO) on EVLW in sheep with early acute respiratory distress syndrome (ARDS).

**Methods** The sheep ARDS model was induced by infusion of endotoxin intravenously, then divided into the ARDS model group ($n = 12$), PEEP group ($n = 21$) and dobutamine group ($n = 13$). The PEEP group was divided into three subgroups: PEEP 5 $cmH_2O$ group ($n = 7$), PEEP 10 $cmH_2O$ group ($n = 8$) and PEEP 15 $cmH_2O$ group ($n = 6$). EVLW was measured by the single indicator thermodilution technique. The EVLW, hemodynamics and lung mechanics parameters were observed at 6 hours after the sheep ARDS model was induced, 2 hours after they received mechanical ventilation with PEEP (5, 10, 15 $cmH_2O$), respectively, and 2 hours after CO increase > 50% of the base value (induced by dobutamine infusion).

**Results** (1) When ARDS was induced in sheep, EVLW increased from 12.8 ± 4.7 ml/kg to 18.1 ± 7.1 ml/kg ($P < 0.01$), and EVLW had no significant change ($P > 0.05$) during the early phase of ARDS (6 hours). The $PaO_2/FiO_2$ was 136.8 ± 34.9 mmHg at ARDS 0 hours, which was higher than that before infusion of endotoxin (444.3 ± 127.7 mmHg, $P < 0.01$). EVLW had no relationship with $PaO_2/FiO_2$, but EVLW after the ARDS model was induced had good correlation with $PaO_2/FiO_2$ ($r = -0.501$, $P < 0.001$). When ARDS was induced, static lung compliance decreased from 26.9 ± 8.4 to 16.4 ± 5.0 ($P < 0.01$). (2) After mechanical ventilation with PEEP for 2 hours, EVLW values in the PEEP 10 $cmH_2O$ group and PEEP 15 $cmH_2O$ group were 14.7 ± 4.5 ml/kg and 15.3 ± 3.7 ml/kg, respectively, which was significantly less than that before applied PEEP (16.5 ± 4.7 ml/kg and 18.4 ± 6.0 ml/kg, respectively; all $P < 0.05$). But EVLW in the 5 $cmH_2O$ group was no different during 2 hours PEEP application. (3) After CO increase > 50% of the base value at 1 hour and 2 hours, EVLW values were 16.3 ± 4.9 ml/kg and 16.9 ± 6.9 ml/kg, respectively, which did not differ from that of the base value (15.1 ± 4.6 ml/kg; all $P > 0.05$).

**Conclusions** EVLW in ARDS sheep increased significantly and remained at the same level during the early phase of ARDS. PEEP had a marked effect on reducing EVLW and the increase of CO induced by dobutamine did not significantly raise the EVLW.

### P94

### Pulmonary surfactant function in patients with acute lung injury/acute respiratory distress syndrome treated by mechanical ventilation

**E Miller[1], M Pirozynski[1], J Jastrzebski[1], M Pawelec[2], T Sosnowski[2]**
*[1]Medical Centre of Postgraduate Medicine, Warsaw, Poland;*
*[2]Warsaw University of Technology, Warsaw, Poland*
*Critical Care* 2005, **9(Suppl 1):**P94 (DOI 10.1186/cc3157)

**Aim** The evaluation of the quality and surface active properties of surfactant carried out *in vitro* in setting the bubble, that is pulsating, with the use of a surfactometer (Pulsating Bubble Surfactometer).

**Materials and methods** Patients requiring mechanical ventilation were enrolled to the study. All patients met the criteria for acute lung injury (ALI) or acute respiratory distress syndrome, according to the American–European Consensus Conference. Additionally, the Lung Injury Score criteria to determine the severity and the course of lung injury were used. Sixty-five patients were included in the study – 45 with respiratory insufficiency, of the latter 30 with indirect ALI and 15 with direct ALI. Twenty patients were included in the reference group. All patients underwent bronchoscopy and bronchoalveolar lavage. The procedures were carried out during the first 24 hours of mechanical ventilation. Analysis of pulmonary surfactant activity was carried out using Pulsating Bubble Surfactometer (Electronetics Corp., USA). Changes of value of the surface tension in the cycle compression–expansion, minimum value of the surface tension, maximum value surface tension and the hysteresis loop changes of the surface tension measured as their area value changes were measured. The normalized hysteresis area, the stability index and the rate of effectiveness of reducing the surface tension were calculated.

**Results** Differences were seen between groups with direct ALI and indirect ALI and the control group, with reference to separate analyses parameters. Minimum value of the surface tension ($P < 0.001$) and maximum value of the surface tension ($P < 0.002$) were significantly lower in the control group, whereas the normalized hysteresis area ($P < 0.001$), the stability index ($P < 0.001$) and the rate of effectiveness of reducing the surface tension ($P < 0.02$) were significantly higher.

Comparison of separate groups revealed significantly lower values of the minimum value of the surface tension ($P < 0.003$), the

normalized hysteresis area ($P < 0.001$), the stability index ($P < 0.007$) and the rate of effectiveness of reducing the surface tension ($P < 0.003$) in the group with direct ALI, compared with the group with indirect ALI. There were no differences in relation to maximum values of the surface tension ($P = 0.135$).
**Conclusions** (1) Pulmonary surfactant dysfunction was observed in the early phase ALI. (2) Direct lung injury was associated with higher impairment of surfactant function than indirect lung injury. (3) Correlation exists between the level of the lung injury and dynamic surface active properties of pulmonary surfactant.

## P95

### Alveolar fibrinolysis is not altered by mechanical ventilation in humans with healthy lungs

**G Choi, E Wolthuis, P Bresser, M Levi, T van der Poll, M Dzoljic, M Vroom, M Schultz**
*Academic Medical Center, Amsterdam, The Netherlands*
*Critical Care* 2005, **9(Suppl 1):**P95 (DOI 10.1186/cc3158)

**Introduction** Mechanical ventilation (MV) aggravates pulmonary inflammation in patients with acute lung injury. Pulmonary inflammation is characterized by alveolar fibrin depositions, which is the net result of increased thrombin-mediated generation of fibrin and upregulation of plasminogen activator inhibitor (PAI), inhibiting fibrin degradation. We recently showed that injurious MV (using high pressures) induces PAI-1 upregulation in rats, thereby limiting pulmonary fibrinolytic activity. In the present study we determine the influence of MV on alveolar PAI-1 expression in humans with healthy lungs.
**Methods** Patients with healthy lungs expected to be mechanically ventilated for ≥ 5 hours (elective surgery) were randomized to a MV strategy using either a tidal volume ($V_T$) of 12 ml/kg and zero positive end expiratory pressure ($HV_T$/ZEEP) or $V_T$ 6 ml/kg and 10 $cmH_2O$ PEEP ($LV_T$/PEEP). Bronchoalveolar lavage (BAL) was performed directly after initiation of MV, and repeated in the contralateral lung after 5 hours of MV. Pulmonary thrombin generation was quantified by measuring thrombin–antithrombin complexes (TATc) in the BAL fluid; fibrinolytic activity by determining plasminogen activator activity (PAA), PAI-1, and tissue-type plasminogen activator (tPA).
**Statistics** Within groups, Wilcoxon signed-rank test; between groups, Mann–Whitney U test. Data are presented as medians with interquartile ranges.
**Results** Nine patients were randomized to $HV_T$/ZEEP, 11 patients to $LV_T$/PEEP. There were no differences in baseline characteristics or outcome. After 5 hours, patients ventilated with $HV_T$/ZEEP showed an increase in alveolar thrombin generation (TATc: 0.91 [0.82–0.98] ng/ml vs 0.75 [0.67–0.81] ng/ml at baseline, $P < 0.01$), in contrast to those with $LV_T$/PEEP (0.84 [0.74–0.91] ng/ml vs 0.81 [0.72–0.87] ng/ml, not significant [NS]). Pulmonary PAI-1 levels did not change ($LV_T$/PEEP: 2.0 [1.6–2.2] ng/ml vs 1.9 [1.8–2.1] ng/ml, NS; $HV_T$/ZEEP: 2.1 [1.8–2.1] ng/ml vs 2.0 [1.7–2.4] ng/ml, NS). Moreover, alveolar PAA was unaffected in both groups ($LV_T$/PEEP: 106 [102–113]% vs 100 [97–105]%, NS; $HV_T$/ZEEP: 102 [97–110]% vs 102 [100–104]%, NS), although levels of tPA increased more with $HV_T$/ZEEP MV ($LV_T$/PEEP: 0.84 [0.65–0.98] ng/ml vs 0.61 [0.55–0.63] ng/ml, $P < 0.001$; $HV_T$/ZEEP: 0.70 [0.70–0.90] ng/ml vs 0.50 [0.40–0.55] ng/ml, $P < 0.01$; between groups, NS).
**Conclusion** Despite upregulation of tPA, alveolar PAA is not altered during 5 hours of MV in patients with healthy lungs. Disturbed alveolar fibrin turnover during MV in healthy lungs seems solely the result of activation of coagulation.

## P96

### Effect of lung protective ventilation strategy on extrapulmonary organs inflammatory response in an acute respiratory distress syndrome rabbit model

**H Qiu, Y Yang, Y Yan**
*Nanjing Zhong-Da Hospital, Southeast University, Nanjing, China*
*Critical Care* 2005, **9(Suppl 1):**P96 (DOI 10.1186/cc3159)

**Objective** To evaluate the influence of a lung protective ventilation strategy on extrapulmonary organ inflammatory response in an acute respiratory distress syndrome (ARDS) rabbit model.
**Methods** The ARDS rabbit models were duplicated by alveoli-lavaged saline. The rabbit were divided into six groups: (1) normal, (2) ARDS group, (3) low volume (VT) with best end-expiratory pressure (PEEP) (LVBP), (4) normal volume with best PEEP (NVBP), (5) low-volume with high PEEP (LVHP), and (6) high-volume zero PEEP (HVZP). Tumor necrosis factor alpha (TNF-α) and IL-10 levels in liver and intestine homogenates were measured by ELISA and their mRNA expression was measured by RT-PCR.
**Results** In the LVBP group, the mRNA expression of TNF-α and IL-10 in liver was lower than the NVBP, LVHP, and HVZP groups. But there was no difference between LVBP and ARDS groups. TNF-α mRNA expression in the LVHP group was higher than the LVBP group in liver tissue, but significantly lower than the HVZP group. Compared with the LVBP group, the TNF-α and IL-10 concentrations in liver were increased markedly in NVBP, LVHP, and HVZP. But there was no difference between the LVBP and ARDS groups. Live TNF-α and IL-10 concentrations were highest in the HVZP group, which was higher than the LVBP and LVHP groups. In the LVBP group, the mRNA expression of TNF-α and IL-10 in intestine was lower than the NVBP, LVHP, and HVZP groups. But there was no difference between the LVBP and ARDS groups. As compared with the LVBP group, the TNF-α and IL-10 concentrations of intestine in NVBP, LVHP, and HVZP were increased markedly, but there was no difference between the LVBP and ARDS groups.
**Conclusions** A lung protective ventilation strategy can downregulate inflammatory mediator expression in the liver and intestine of ARDS rabbits and may prevent the occurrence of multiple organ dysfunction syndrome.

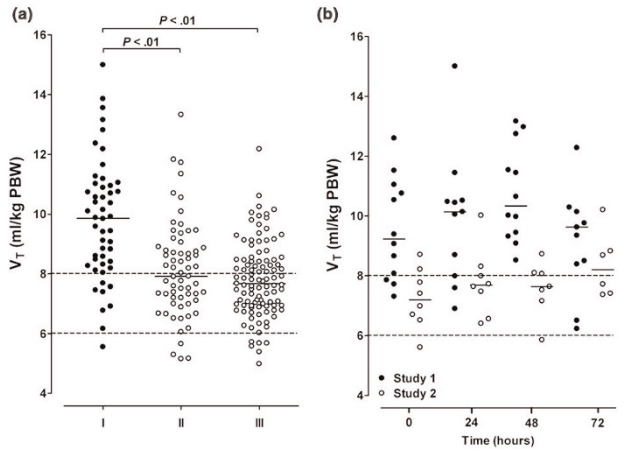
## P97

### Persistent use of lower tidal volumes after a simple intervention consisting of feedback and education

**E Wolthuis[1], R Determann[1], M Vroom[1], J Kesecioglu[2], M Schultz[1]**
*[1]Academic Medical Centre, Amsterdam, The Netherlands; [2]UMC, Utrecht, The Netherlands*
*Critical Care* 2005, **9(Suppl 1):**P97 (DOI 10.1186/cc3160)

**Introduction** Use of lower tidal volumes (Vt) is recommended for patients suffering from ALI/ARDS. We previously reported on a simple 'intervention' aimed at lowering Vt (goal: Vt 6–8 ml/kg): this intervention consisted of feedback and education on the use of lower Vt, during which special attention was paid to the importance of closely adjusting Vt to predicted body weight (PBW) instead of actual body weight. This intervention resulted in a significant decline of Vt in our IC [1].
**Methods** To determine the longstanding effects of the aforementioned intervention: (a) we compared data on Vt before feedback and education (June 2003, $n = 50$, period I) with Vt 15 months later (September 2004, $n = 103$, period III); (b) in addition, we collected data on Vt of patients recruited in two consecutive randomized controlled ALI/ARDS trials: the first trial

**Figure 1 (abstract P97)**




was performed in the 10-month period before the intervention (March 2002–December 2002, $n = 12$), and the second was performed in a 10-month period after the intervention (July 2003–May 2004, $n = 8$).

**Statistical analysis** Mann–Whitney test. $P < 0.05$ was considered significant.

**Results** (a) Before intervention, Vt was 9.4 (IQR: 8.2–10.8) ml/kg PBW; Vt declined shortly after the intervention and remained low (7.7 [6.9–8.5] ml/kg PBW) 15 months after the intervention (Fig. 1a); (b) Vt in the second randomized controlled trial was significantly lower as compared with Vt in the first study on ALI/ARDS patients (Fig. 1b).

**Conclusions** Feedback and education caused a persistent decline in Vt in our IC. These results possibly underscore the use of PBW, instead of actual body weight, to adjust Vt.

**Reference**

1. Wolthuis, *et al.*: *Intensive Care Med*, in press.

## P98

### How did randomized trials impact mechanical ventilator setting in our unit?

**D Chiumello, E Noè, L Ghisoni, B Lavelli, M Cressoni, M Racagni, L Landi, P Taccone**
*Policlinico IRCCS, Milan, Italy*
*Critical Care* 2005, **9(Suppl 1):**P98 (DOI 10.1186/cc3161)

Mechanical ventilation (MV) is the principle supportive care in ALI/ARDS patients. MV can be associated with several negative side effects and lung injury (VILI). In recent years several randomized trials tried to focus the optimal ventilatory strategy in ALI/ARDS patients aimed to avoid or minimize the VILI [1–3]. In this study we evaluated how MV has been employed in recent years in ALI/ARDS patients in our intensive care unit (eight beds). We retrospectively collected data of all ALI/ARDS patients, from 2001 to August 2004. To be included in the study the patient must to be ventilated for at least 48 hours without an unfavorable short-term prognosis. Sixty-two patients were enrolled; the mean age and the body mass index were not different between the years (54 ± 17, 62 ± 12, 56 ± 16 and 55 ± 20 years and 24 ± 3, 24 ± 2, 25 ± 6 and 25 ± 4 kg/m$^2$, respectively). The variables in Table 1 were not different at day 3 and day 7 between the four years. We did not find any difference in our 'local' lung ventilatory setting through the years regarding level of PEEP or tidal volume. Instead, to set the tidal volume based on body weight we prefer to set taking into account the airway plateau pressure.

**Table 1**

| Year | 2001 | 2002 | 2003 | 2004 |
|---|---|---|---|---|
| Patients (*n*) | 14 | 16 | 21 | 11 |
| $PaO_2/FiO_2$ | 189 ± 74 | 134 ± 77 | 173 ± 64 | 146 ± 63 |
| Tidal volume (ml/kg) | 9.9 ± 1.9 | 8.5 ± 2.1 | 9.9 ± 1.8 | 10.1 ± 2.5 |
| Airway plateau pressure ($cmH_2O$) | 26 ± 6 | 27 ± 6 | 27 ± 6 | 27 ± 4 |
| PEEP ($cmH_2O$) | 8 ± 3 | 10 ± 4 | 9 ± 4 | 9 ± 4 |
| Primary ARDS | 11 (79%) | 12 (75%) | 12 (57%) | 3 (27%) |
| ICU stay (days) | 35 ± 21 | 37 ± 28 | 36 ± 35 | 32 ± 25 |
| Mortality | 3 (21%) | 8 (50%) | 8 (38%) | 3 (27%) |

**References**

1. Acute Respiratory Distress Syndrome Network: *N Engl J Med* 2000, **342:**1301-1308.
2. Amato M, *et al.*: *N Engl J Med* 1998, **338:**347-354.
3. Ranieri VM, *et al.*: *JAMA* 1999, **282:**54-61.

## P99

### Ventilation according the open lung concept attenuates pulmonary dysfunction after cardiac surgery

**D Reis Miranda, P Koetsier, A Struys, R van Thiel, A Bogers, B Lachmann, D Gommers**
*Erasmus MC, Rotterdam, The Netherlands*
*Critical Care* 2005, **9(Suppl 1):**P99 (DOI 10.1186/cc3162)

**Introduction** After cardiac surgery, pulmonary dysfunction may develop as shown by a significant reduction of functional residual capacity (FRC) after extubation [1]. We hypothesized that ventilation according to the open lung concept (OLC) attenuates FRC reduction after extubation.

**Methods** Sixty-three patients undergoing cardiopulmonary bypass were randomly assigned into three groups: conventional mechanical ventilation (CMV); OLC before, during and after cardiothoracic surgery (early open lung [EOL]); and CMV during surgery, OLC on the intensive care unit (late open lung [LOL]). The CMV group was ventilated with low tidal volume (6–8 ml/kg) with 5 $cmH_2O$ PEEP. During OLC ventilation, recruitment maneuvers were applied until $PaO_2/FiO_2$ was above 50 kPa. This was maintained by the use of sufficient levels of PEEP. FRC was measured preoperatively and 1, 3 and 5 days after extubation. Peripheral oxygen saturation ($SpO_2$) was measured after extubation, breathing room air. $SpO_2 < 91\%$ was defined as hypoxia. Serum IL-8 was measured after aortic cross-clamp release. The variables were compared using analysis of variance for repeated measurements.

**Results** Compared with the CMV group, FRC was significantly higher in the EOL group. In the LOL group, FRC was only significantly higher than the CMV group on the first day after extubation. In the CMV group, 37% of the patients were hypoxic on the third day after extubation, whereas none of the patients of both OLC groups. After release of the aortic cross clamp, IL-8 decreased significantly faster in the early OLC group compared with the CMV group.

**Conclusion** Especially early application of the OLC group attenuated postoperative pulmonary dysfunction, measured by FRC and the occurrence of postoperative hypoxemia. This is probably founded on an attenuated pulmonary inflammation, as shown by a faster decrease of serum IL-8 concentration during early application of OLC.

**Reference**
1. Ng CS, Wan S, Yim AP, Arifi AA: **Pulmonary dysfunction after cardiac surgery.** *Chest* 2002, **121:**1269-1277.

## P100

### Effects of positive end-expiratory pressure on liver function and splanchnic microcirculation

**A Holland, O Thuemer, C Schelenz, S Sakka**
*Friedrich-Schiller-University, Jena, Germany*
*Critical Care* 2005, **9(Suppl 1):**P100 (DOI 10.1186/cc3163)

**Introduction** The effects of positive end-expiratory pressure (PEEP) on liver function and blood flow in experimental and clinical studies revealed non-uniform results. In this clinical study, we investigated the effects of PEEP on liver function (indocyanine green plasma disappearance rate [ICG-PDR]) and splanchnic microcirculation as estimated by regional $PCO_2$ ($PRCO_2$) using gastric tonometry.
**Methods** With approval by our local ethics committee and written consent, we studied 14 patients after elective coronary bypass surgery using extracorporal circulation (13 males, one female; age 48–74, mean 63 ± 7 years). All patients underwent extended hemodynamic monitoring by a pulmonary artery catheter for clinical indication. ICG-PDR and gastric mucosal $PRCO_2$ were assessed on ICU admission (PEEP 5 mbar), 2 hours after increasing PEEP to 10 mbar and again after 2 hours at PEEP 5 mbar. In addition, the cardiac index, central venous pressure (CVP) and left atrial pressure (LAP) were measured. All patients were on pressure-controlled ventilation and the inspiratory peak pressure was adapted to maintain $PaCO_2$ constant. Vasoactive drugs, blood pressure, minute volume and sedation were kept constant.
**Results** The cardiac index significantly increased during the study. However, there was a trend for ICG-PDR to change between the different time points ($P = 0.05$). However, the difference between regional and arterial $PCO_2$ (PCO2-gap) significantly increased following PEEP5 (1) and remained higher at PEEP5 (2) than at PEEP5 (1) (Table 1).

**Table 1**

| | PEEP5 (1) | PEEP10 | PEEP5 (2) |
|---|---|---|---|
| CI (l/min/m$^2$) | 2.7 ± 0.5 | 3.0 ± 0.6* | 3.1 ± 0.4* |
| CVP (mmHg) | 8 ± 4 | 9 ± 3 | 8 ± 3 |
| LAP (mmHg) | 7 ± 3 | 9 ± 3 | 8 ± 3 |
| PDR (%/min) | 24.0 ± 6.9 | 22.0 ± 7.9 | 25.3 ± 7.8 |
| $PCO_2$-gap (kPa) | 0.2 ± 0.9 | 1.1 ± 1.0* | 0.9 ± 1.0* |

*$P < 0.05$ vs PEEP5 (1) (analysis of variance).

**Conclusion** Increasing PEEP from 5 to 10 mbar was accompanied with a trend towards a decrease in liver function and blood flow (ICG-PDR). The changes in $PCO_2$-gap were within the physiological range and of no clinical relevance. An increase in PEEP from 5 to 10 mbar can be applied without compromising liver blood flow and function and splanchnic microcirculation.

## P101

### Linear and nonlinear analysis of respiratory resistance in ARDS patients

**F Frantzeskaki[1], A Betrosian[1], A Amygdalou[2], M Vassileiou[3], P Behrakis[4]**
*[1]Ippokration General Hospital of Athens, Greece; [2]Red Cross Hospital, Athens, Greece; [3]University of Ioannina, Medical School, Ioannina, Greece; [4]University of Athens, Medical School, Athens, Greece*
*Critical Care* 2005, **9(Suppl 1):**P101 (DOI 10.1186/cc3164)

**Purpose** We analyzed during the whole respiratory cycle the resistance, elastance, and flow dependence of resistance in ARDS patients, at three levels of PEEP, using two different models: linear modeling, and nonlinear modeling for flow dependence of resistance.
**Methods** Airway opening pressure (P), flow (V′) and volume (V) signals were recorded in 18 patients with ARDS and in 15 patients without known respiratory disorder (control group), all artificially ventilated, at three levels of PEEP (0, 5, and 10 hPa). Data were analyzed using multiple linear regression analysis according to the equations: $P = Ers*V + Rrs*V' + Po$, and (b) $P = Ers*V + (k1 + k2*V\alpha')*V' + Po$, where Ers and Rrs represent the respiratory system elastance and resistance, k1 the linear coefficient of resistance, k2 the flow-dependent coefficient of resistance, and Po the end expiratory pressure.
**Results** The respiratory resistance (controls: $P = 0.01$, ARDS: $P = 0.001$), the linear coefficient of resistance (controls: $P = 0.05$, ARDS $P = 0.02$) and the flow-dependent coefficient of resistance (controls: $P = 0.04$, ARDS: $P = 0.04$) were diminished significantly with the application of PEEP in both groups of patients, especially at a high level of PEEP (10 hPa). All the measured mechanical parameters were significantly higher in the ARDS group compared with the controls.
**Conclusion** Mechanical ventilation with PEEP application in ARDS patients is related to a decline of linear and nonlinear coefficients of respiratory resistance, during the respiratory cycle. More complex models accounting for the flow dependence of resistance may improve the accuracy of measurements of respiratory mechanics and offer more efficient mechanical ventilation in ARDS patients.

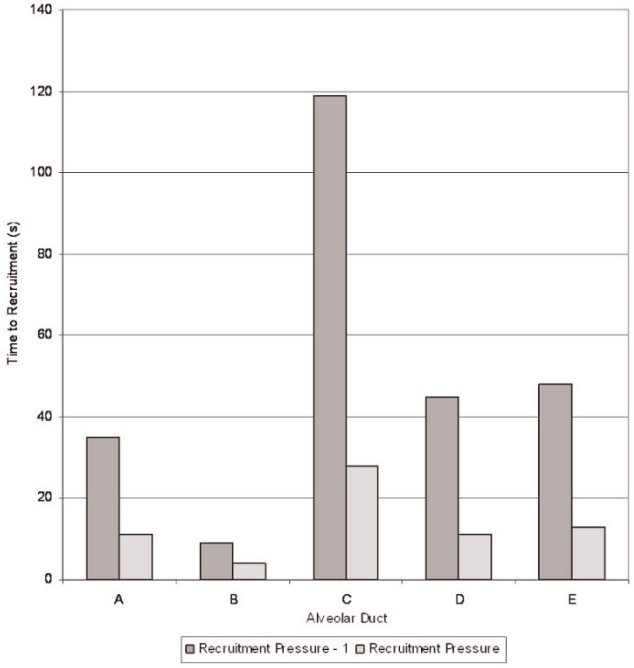
## P102

### Temporal effect of applied pressures on observed alveolar recruitment

**J DiRocco[1], D Carney[1], L Gatto[2], S Landas[1], G Nieman[1]**
*[1]Upstate Medical University, Syracuse, NY, USA; [2]SUNY – Cortland, NY, USA*
*Critical Care* 2005, **9(Suppl 1):**P102 (DOI 10.1186/cc3165)

**Introduction** Lung recruitment has been hypothesized to be an important component of protective ventilatory strategy in acute respiratory distress syndrome. Determination of optimal recruitment strategies is limited by uncertainty regarding the relationship between time, pressure, and recruitment at the alveolar level. In this study, we assessed the temporal characteristics of alveolar recruitment.
**Methods** Rats were subjected to saline lavage lung injury. *In vivo* microscopy identified five separate alveolar sacs for which individual recruitment pressures (RP) were determined by increasing the continuous positive airway pressure (CPAP). The time to recruitment was recorded upon application of three pressures for a maximum of 120 s: RP, RP – 1 $cmH_2O$, and RP – 2 $cmH_2O$. Volume history was normalized before each pressure application.

**Figure 1 (abstract P102)**




**Results** No recruitment was observed in the 2-min time period with a pressure of RP – 2 $cmH_2O$. The time to recruitment was significantly shorter with application of RP vs RP – 1 $cmH_2O$ (Fig. 1). Significance was determined by a one-tailed, paired *t* test, $P < 0.03$.

**Conclusions** We were able to directly observe recruitment behavior that exhibited sensitivity around a critical opening pressure with marked changes in time to recruitment with small changes in pressure. This suggests that very small differences in the airway pressures (as small as 1 $cmH_2O$ in this study) may have dramatic alterations in lung recruitment.

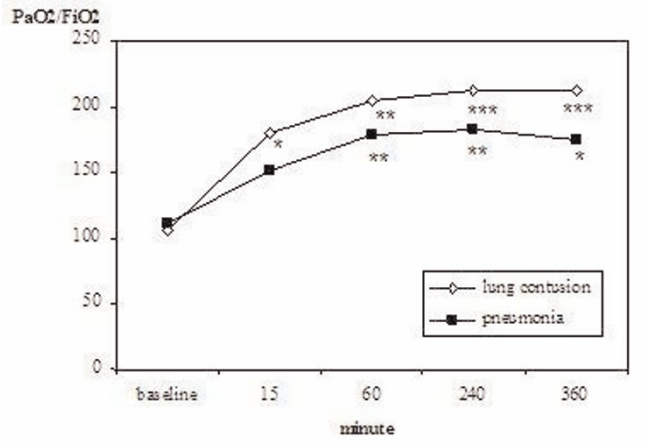
## P103

### The effects of sustained inflation and post-inflation PEEP in acute respiratory distress syndrome due to pneumonia and traumatic lung contusion

**S Kizilirmak, S Tugrul, N Cakar, P Ergin Ozcan, F Esen, L Telci**
*Istanbul Universitesi, Istanbul Tip Fakultesi, Istanbul, Turkey*
*Critical Care* 2005, **9(Suppl 1):**P103 (DOI 10.1186/cc3166)

**Objective** To investigate the response to a sustained inflation (SI) and post-inflation PEEP (PI-PEEP) in acute respiratory distress syndrome (ARDS) due to pneumonia and traumatic lung contusion.

**Figure 1 (abstract P103)**




**Methods** Twenty-five patients with ARDS were enrolled (pneumonia $n = 13$, lung contusion $n = 12$). During baseline ventilation, 7 ml/kg tidal volume, 12–15 breaths/min respiratory rate and an I:E ratio of 1:2 were used. SI was performed by 45 $cmH_2O$ continuous positive airway pressure for 30 s. PI-PEEP was titrated decrementally starting from 20 $cmH_2O$ in order to find the best PEEP. $FiO_2$ was decreased under baseline ventilation. If the peak inspiratory pressure exceeded 45 $cmH_2O$ with 20 $cmH_2O$ PEEP, the PEEP was reduced by 1 $cmH_2O$ decrements. Blood gas analyses were performed at baseline, 15th minute, first hour, fourth hour and sixth hour after SI.

**Results** Demographic data are presented in Table 1. PI-PEEP levels were set at 16.1 ± 1.6 $cmH_2O$ in the pneumonia group and 15.9 ± 3.1 $cmH_2O$ in the lung contusion group ($P = 0.9$). Following SI, the $PaO_2/FiO_2$ ratio improved in all of the patients (Table 2 and Fig. 1).

**Table 1 (abstract P103)**

| | Pneumonia | Lung contusion | Mann–Whitney U |
|---|---|---|---|
| APACHE II | 20.7 ± 7.5 | 13.5 ± 9.0 | 0.01 |
| LIS | 2.75 ± 0.6 | 2.63 ± 0.5 | 0.7 |
| MOF | 6.2 ± 3.3 | 4.9 ± 3.8 | 0.2 |

**Conclusions** SI followed by high levels of PI-PEEP provided an increase in arterial oxygenation in both ARDS forms. However, this strategy was found to be more effective in improving arterial oxygenation in the lung contusion group. This finding might address the idea that physiopathology of two pulmonary insults of ARDS presents in different forms.

**Table 2 (abstract P103)**

| | Baseline | 15th minute | First hour | Fourth hour | Sixth hour | ANOVA (*P*) |
|---|---|---|---|---|---|---|
| Pneumonia | 111 ± 31 | 151 ± 53 | 179 ± 76** | 183 ± 90** | 175 ± 71* | 0.0015 |
| Lung contusion | 106 ± 29 | 180 ± 66* | 205 ± 70** | 213 ± 92*** | 213 ± 116*** | 0.0002 |

* $P < 0.05$, ** $P < 0.01$ and *** $P < 0.001$.

## P104

### Use of a sigmoidal equation to analyze the pressure–volume curve obtained by the low flow method

**V Tomicic, L Fidanza, M Espinoza, J Graf, C Canals**
*Clínica Alemana de Santiago, Santiago de Chile, Chile*
*Critical Care* 2005, **9(Suppl 1):**P104 (DOI 10.1186/cc3167)

**Introduction** The adjustment of PEEP and tidal volume to the lower inflection point and upper inflection point of the P–V curve, respectively, has been proposed to optimize mechanical ventilation in ARDS. Usually, the P–V curve is analyzed by eye from a graph, with high variability. Venegas and colleagues [1] developed a sigmoidal equation that fits remarkably well to P–V curves obtained by the supersyringe method. Our objective was to determine whether this equation is able to model P–V curves obtained by the low flow method.
**Methods** The P–V curve was obtained by the low flow method using a Servo Siemens 300 ventilator [2]. Pressure and flow signals were obtained from the analog port (N81) and converted to digital format through a PCMCIA card (Measurement Computing, PC-CARD DAS 16/12). A program was developed to acquire, display, save, and analyze pressure and volume signals from the ventilator. The sigmoidal equation has four fitting parameters: (a) lower asymptote (volume); (b) distance from lower asymptote to upper asymptote (inspiratory capacity); (c) true inflection point (pressure); and (d) range of pressure from (c) to the point of high compliance. The equation is fitted to the P–V data by the least mean square (LMS) algorithm to minimize the sum of squared residuals. After iteration, the best fit correlation ($R^2$) between real curves and those obtained from the equation was calculated. From the fitted equation, three points of interest were defined: the inflection point (c), where the first derivative has a maximum and the second derivative has a zero; the point of maximal compliance increase (Pmci), where the rate of change of upward slope is maximal or where the second derivative of the function has a maximum (calculated as (c) – 1.317 (d)); and the point of maximal compliance decrease (Pmcd), where rate of change of downward slope is maximal or where the second derivative of the function has a minimum (calculated as (c) + 1.317 (d)).
**Results** The inspiratory limb of low flow P–V curves were obtained from six mechanically ventilated ARDS patients. The mean $R^2$ value between the ventilator volume signal and the volume predicted by the fitted curves was 0.996 ± 0.002 (standard deviation).
**Conclusions** The sigmoidal equation described by Venegas and colleagues fits well to P–V curves obtained by the low flow method. Our system may contribute to improve the evaluation of respiratory mechanics and to adjust mechanical ventilation settings at the bedside in ARDS patients.
**References**
1. Venegas, *et al.*: *J Appl Physiol* 1998, **84:**389-395.
2. *Am J Respir Crit Care Med* 1999, **159:**275-282.

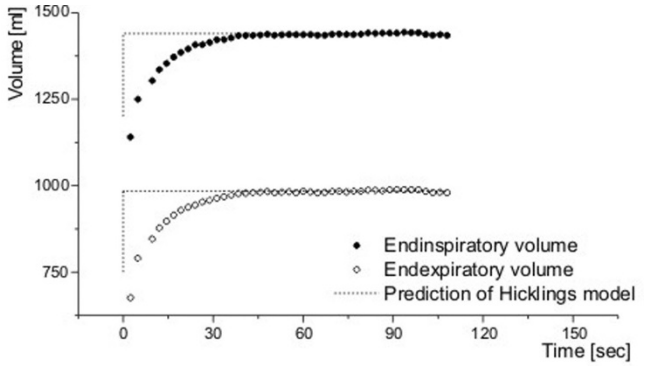
## P105

### Modeling time effects of recruitment and P–V curve characteristics: a simulation study

**K Möller[1], C Stahl[2], J Guttmann[2]**
*[1]University of Applied Sciences, Villingen-Schwenningen, Germany; [2]University of Freiburg, Germany*
*Critical Care* 2005, **9(Suppl 1):**P105 (DOI 10.1186/cc3168)

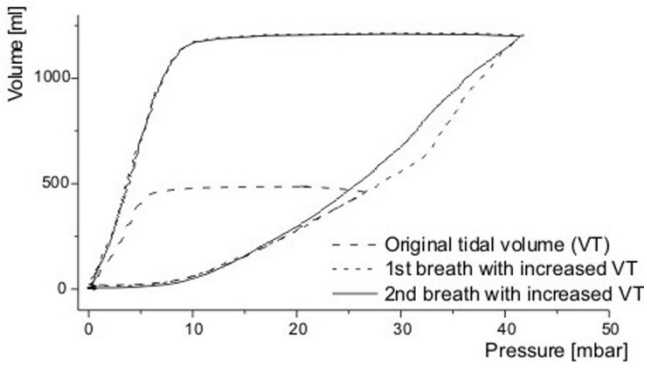
**Introduction** In a multicenter study on respiratory mechanics in ALI and ARDS [1] we observed phenomena most probably related to time effects: change in compliance after a recruitment maneuver, transient end-expiratory volume (Fig. 1) after changing PEEP, and a transient change in shape of the P–V curve after a change in tidal volume (Fig. 2). To gain a better understanding of temporal effects we developed a mathematical model of the respiratory system to investigate these phenomena.
**Methods** We extended the model of recruitment proposed by Hickling [2] to include chest wall characteristics, FRC, and an initial opening volume of alveolar units once recruited. Alveolar units had a nonlinear compliance and were organized in a bronchial tree structure. Depending on the position in the tree each lung unit was exposed to a gravitational superimposed pressure from 0 in the ventral compartment to a maximal value in the dorsal compartment. Opening and closing pressures of lung units were normally distributed with a modifiable mean and standard deviation. Time dependency was modeled by including timing parameters for recruitment and derecruitment of alveolar units similar to the approach of Bates and colleagues [3].
**Results** In contrast to Hickling's model, simulations with the extended model produced realistic transients in volume. Furthermore, transient changes in compliance were predicted by the model. Modeling of recruitment and derecruitment as time-

**Figure 1 (abstract P105)**




Observed transient volume after switching from ZEEP to PEEP 18 in an ARDS patient. End expiratory volume at ZEEP was defined as 0.

**Figure 2 (abstract P105)**




Transient in the shape of the P–V curve after an increase in tidal volume.

dependent phenomena allowed one to mimic the transients as observed in ARDS patients.

**Conclusion** The shape of simulated P–V loops is influenced by time effects only related to closing and opening of alveolar units. Up to now, transient effects have been explained by viscoelasticity and by mechanical inhomogeneity. From the present study we conclude that timing effects during recruitment may be a third mechanism of transient mechanical behaviour of the respiratory system.

**References**

1. Stahl, *et al.*: *Critical Care* 2004, **8(suppl 1):**P28.
2. Hickling: *Am J Respir Crit Care Med* 1998, **158:**194-202.
3. Bates, *et al.*: *J Appl Physiol* 2002, **93:**705-713.

## P106

### How to choose the duration of prone-position ventilation between patients with acute respiratory distress syndrome caused by pulmonary and extrapulmonary disease?

**Y Huang, H Qiu, L Liu**
*Department of Critical Care Medicine, Zhong-da Hospital and School of Clinical Medicine, Southeast University, Nanjing, China*
*Critical Care* 2005, **9(Suppl 1):**P106 (DOI 10.1186/cc3169)

**Objectives** To determine the different effect of prone-position ventilation (PPV) in patients with acute respiratory distress syndrome (ARDS) resulting from a pulmonary cause (ARDSp) and that from an extrapulmonary cause (ARDSexp) on oxygenation, respiratory mechanics and hemodynamics. To choose the duration of ventilation in the prone position in the two groups.

**Methods** Nine ARDSp patients and seven ARDSexp patients within 3 days of onset of ARDS were included in this study, which were classified as two groups. Patients were placed in prone position for 2 hours. The effect of different times (pre-PPV, PPV 0.5 hours, PPV 2 hours) on oxygenation, respiratory mechanics and hemodynamics were observed. Lung computerized tomography (CT) was obtained in both the supine position and 10 min after turning to the prone position.

**Results** Compared with pre-PPV, in ARDSp the $PaO_2/FiO_2$ was not increased after 0.5 hours, and increased only after 2 hours in the prone position (130.6 ± 36.2 mmHg to 165.1 ± 72.3 mmHg, $P < 0.05$). But in ARDSexp, $PaO_2/FiO_2$ was significantly increased after 0.5 hours and 2 hours in the prone position (116.5 ± 55.0 mmHg to 163.2 ± 46.4 mmHg and 182.7 ± 87.7 mmHg, $P < 0.05$). After 0.5 hours in the prone position the responding ratio of ARDSexp was higher than ARDSp (100% vs 11.1%, $P = 0.0007$). After 2 hours, no significant difference of responding ratio was found between the two groups (85.7% vs 66.7%, $P = 0.392$). The changes of the $PO_2$ were similar to the $PaO_2/FiO_2$. The $PCO_2$ and the Cst,rs did not differ significantly between the prone position and the supine position in the two groups. In ARDSp, the Raw was 10.8 ± 1.4 $cmH_2O/s/l$ in the supine position, and it was significantly decreased after 2 hours in the prone position (8.4 ± 1.8 $cmH_2O/s/l$) ($P < 0.05$). Chest CT scans of ARDSp and ARDSexp patients were markedly different.

**Conclusions** PPV could be used to improve severe hypoxemia of ARDS. It improved the $PaO_2/FiO_2$ ratio rapidly in ARDSexp, but should prolong the period in ARDSp.

## P107

### PEEP and prone ventilation in liver transplantation: consideration or contraindication?

**E Sykes, C O'Suilleabhain, I Nesbitt, J Cosgrove**
*Freeman Hospital, Newcastle Upon Tyne, UK*
*Critical Care* 2005, **9(Suppl 1):**P107 (DOI 10.1186/cc3170)

**Introduction** Acute respiratory distress syndrome (ARDS) can complicate liver transplantation (LT). Positive end expiratory pressure (PEEP) and prone ventilation (PV) have theoretical adverse hepatic effects. An adult paracetamol overdose required super-urgent LT. Immediate postoperative hypoxaemia due to ARDS developed (Table 1, i), as supported by $FiO_2/PaO_2$ ratio, bilateral pulmonary infiltrates, and normal pulmonary artery occlusion pressures. PEEP (15cm $H_2O$) and PV improved gas exchange immediately (Table 1, ii) and at 18 hours (Table 1, iii). Doppler examination of hepatic vessels was normal. Discharge home was on day 41.

**Table 1**

| | $FiO_2$ | pH | $PaCO_2$ (kPa) | $PaO_2$ (kPa) | Lactate (mmol/l) | Cardiac index (l/min/m$^2$) |
|---|---|---|---|---|---|---|
| i | 1.0 | 7.15 | 6.4 | 6.0 | 12.3 | 4.30 |
| ii | 1.0 | 7.279 | 5.5 | 21.6 | 6.4 | 4.27 |
| iii | 0.5 | 7.408 | 5.8 | 11.3 | 3.2 | 3.06 |

**Methods** A telephone questionnaire to British LT intensive care units about using PEEP and PV postoperatively after emergency LT.

**Results** Completed questionnaires were obtained from the six other British LT intensive care units. All responders were consultant intensivists. Four routinely set PEEP on the ventilator. Three stated levels depended on oxygen requirements. One routinely used PEEP irrespectively. Two used PEEP depending on oxygen requirements. Two felt PV was 'absolutely contraindicated', quoting an evidence base, alternative available measures, and concerns regarding hepatic perfusion. No responder could recall PV being used in this context.

**Discussion** Opinions regarding the use of PEEP post emergency LT are mixed. Opinions of PV appear polarised. No units appear to have used it in this context. Potential detrimental effects of PEEP and PV in LT include reduced cardiac output and hepatic blood flow. Increased intra-abdominal pressure with PV may compound this. However, restoring cardiac output maintains normal liver function and blood flow [1,2]. Positioning to allow abdominal excursion minimises risk [2]. Concerns raised in the questionnaire may be overstated. We suggest both modalities can be used effectively, without detriment to donor liver or patient outcome. Further research is required.

**References**

1. Matuschak GM: *J Appl Physiol* 1987, **62:**1377-1383.
2. Hering JR: *Intensive Care Med* 2002, **28:**53-58.

## P108

### Effects of prone position ventilation and kinetic therapy in acute respiratory failure

**J Lewejohann, E Rieh, B Börner, E Muhl, H Bruch**
*Universitätsklinikum Schleswig-Holstein – Campus Lübeck, Germany*
*Critical Care* 2005, **9(Suppl 1):**P108 (DOI 10.1186/cc3171)

**Introduction** In acute respiratory failure (ARF), in particular acute lung injury (ALI) and respiratory distress syndrome (ARDS), change

from the supine position (SP) to the prone position (PP) or the use of kinetic therapy can improve oxygenation by recruiting alveoli situated in dorsal-dependent regions of the lung and by alteration of the ventilation/perfusion ratio. The efficacy of this intervention can be demonstrated by the course of oxygenation index. The aim of our study is to compare prone position ventilation (PP) and kinetic therapy (KT) in the first 5 days after intervention in patients with acute respiratory failure.

**Methods** We studied $n = 149$ patients with ARF at a surgical ICU in a university hospital using the American–European consensus definition in a clinical follow-up design. The physicians on duty had the freedom of choice to use PP or KT guided by their clinical experience. One hundred and eleven patients (ALI: $n = 18$/ARDS: $n = 93$; mean age 66 ± 13 [standard error] years) were ventilated intermittently in SP and PP (135° left/right-side position) for at least 6 hours per day for supportive treatment of respiratory failure. Thirty-eight patients (ALI: $n = 16$/ARDS: $n = 22$; mean age 60 ± 16 [standard error] years) were treated with kinetic therapy using the Rotorest®-bed (60° left/right side; KCl).

Data collection included, apart from baseline characteristics, the individual oxygenation index of the patients in the course of the first 5 days after intervention. The individual oxygenation index before and after intervention was compared with linear regression analysis for each group (linear regression procedure and *t* test; SPSS®).

**Results** During conventional ventilation in the supine position there was no significant improvement in oxygenation in both groups. The mean oxygenation index ($PaO_2/FiO_2$) decreased until intervention to 157.6 ± 0.48 mmHg in the PP group and to 165.8 ± 1.47 mmHg in the KT group (mean ± standard error of the mean). Both forms of positional changes lead to a distinct improvement of oxygenation: after 120 hours the oxygenation index in the PP group was 219.67 ± 0.66 and in the KT group was 197.89 ± 2.07 mmHg. Subsequent to intervention the PP group showed a more rapid and significant increase of oxygenation index in comparison with the KT group as the equations of linear regression show: $y[PPV] = 4.4618 \times X + 188.72$ and $y[KT] = 3.9349 \times X + 160.47$. Mortality was 62.2% in the PP group and 63.2% in the KT.

**Discussion** In ARF the change of body position in the form of PP and KT leads to an improvement of oxygenation. PP seems to have a more rapid and marked effect than KT. It is remarkable that mortality is nearly the same in both groups, despite the unequal group size. PP is a comparatively simple strategy to treat the heterogenity of ventilation and perfusion in ARF and needs no special technical equipment, while KT is an advantageous alternative in patients with contraindications for PP.

## P109

### Is the quantitative analysis of lung computed tomography accurate in ALI/ARDS patients?

**D Chiumello, M Cressoni, M Racagni, A D'Adda, S Azzari, S Terragni**
*Policlinico IRCCS, Milan, Italy*
*Critical Care* 2005, **9(Suppl 1):**P109 (DOI 10.1186/cc3172)

The CT scan allows an accurate morphologic analysis of an 'ARDS' lung. In addition, with the spiral CT it is also possible to perform a quantitative analysis using dedicated software. The quantitative analysis is based on the strict correlation between the X-ray attenuation in a given volume of tissue and the physical density of that volume. The CT is determined by the percentage of radiation that is absorbed by that volume.

However, due to the necessity of a manually drawing of the lung (i.e. to include the lung and to exclude big vessels, trachea, pleural effusion, etc.), it would be possible to increase the inaccuracy of the analysis.

The aim of this study was to evaluate the accuracy of analysis between trained physicians (four medical doctor) and two radiologists. We enrolled 12 intubated sedated paralyzed patients ALI/ARDS patients (mean age 63.5 ± 16.9 years, BMI 24.1 ± 4.7 $m^2$, tidal volume 532 ± 195 ml, PEEP 11.2 ± 1.9 $cmH_2O$, $PaO_2/FiO_2$ 205 ± 57). The CT scan was done for clinical purpose, in static conditions, at end expiration 5 or 15 $cmH_2O$ PEEP and at end inspiration 45 $cmH_2O$ airway pressure. The exposures were taken at 120 KV and 250 mA. The lung volume, weight and the distribution of lung weight between the different parts was measured using the 'Maluna' software (University of Mannheim, Germany).

The results show that the quantitative analysis, although requiring a physician to manually draw the region of interest of the lung, presents a high degree of accuracy.

**Table 1**

| | Physicians | Radiologists |
|---|---|---|
| Total volume (ml) | 3956 ± 1608 | 3598 ± 1654 |
| Total weight (mg) | 1419 ± 471 | 1391 ± 449 |
| Weight hyperinflated | 41 ± 79 | 41 ± 82 |
| Weight inflated | 442 ± 160 | 440 ± 164 |
| Weight poorly | 439 ± 269 | 419 ± 270 |
| Weight not inflated | 496 ± 350 | 489 ± 362 |

## P110

### A validation study of a new software for computed tomography lung measurement

**D Chiumello, M Cressoni, M Racagni, L Landi, A D'Adda, S Azzari, S Terragni**
*Policlinico IRCCS, Milan, Italy*
*Critical Care* 2005, **9(Suppl 1):**P110 (DOI 10.1186/cc3173)

The use of computed tomography (CT) in the management of ALI/ARDS patients is quite common, due to the possible additional clinical information and the influence on the patient's treatment. With the new spiral CT scan it is possible to measure the total lung volume, the percentage of lung tissue and gas, there being a linear correlation between the physical density and the CT coefficient of attenuation.

**Figure 1 (abstract P110)**

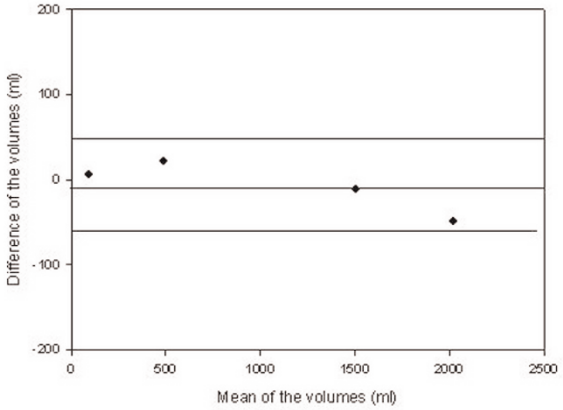
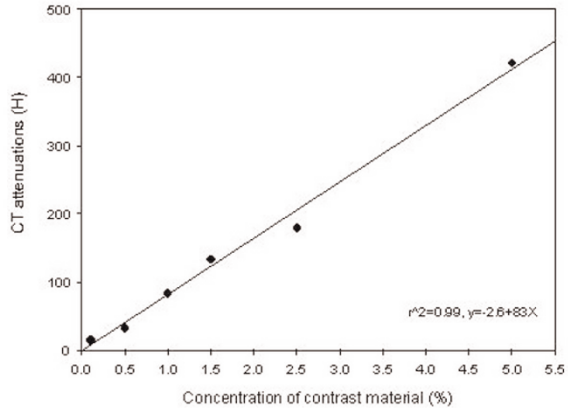


**Figure 2 (abstract P110)**




The aim of this study was to evaluate *in vitro* the new computer program 'Maluna' (University of Mannheim, Germany) dedicated to measuring the lung volume, weight and gas/tissue ratio.
A series of different known volumes of water (100, 500, 1500 and 2000 ml) were studied. In addition, the contrast material was diluted with water to obtain solutions of increasing concentrations (0, 0.5, 1, 1.5, 2.5 and 5%). The spiral CT was performed at 120 KV and 240 mA. Each CT section was manually delineated by a physician. The total volume was computed as the total number of voxels present in a given region times the volume of the voxels, while the CT number was directly related to the physical density.
Figure 1 shows the Bland–Altman analysis between the known volumes of water and the measured volumes by 'Maluna'; Fig. 2 shows the linear regression between the CT attenuation coefficient with increasing concentrations of contrast material in the solution.
These data show that 'Maluna' is able to correctly compute the volumes and CT number.

## P111

### Are three computed tomography lung sections comparable with the whole lung?

**D Chiumello, N Bottino, M Cressoni, M Racagni, L Landi, A D'Adda, F Polli, S Terragni, L Gattinoni**
*Policlinico IRCCS, Milan, Italy*
*Critical Care* 2005, **9(Suppl 1):**P111 (DOI 10.1186/cc3174)

Computed tomography (CT) has been shown to provide accurate measurements of lung tissue mass and volume. However, besides the risk of moving the patient from intensive care to CT scan and the high costs, the high radiological exposure to X-rays may limit the possibility for relatively frequent CT acquisition. One chest CT scan corresponds to 400 chest X-rays [1]. A possible solution to reduce the X-ray exposure could to be perform only three lung sections compared with the whole lung.
The aim of this study was to investigate the difference between the three CT slices technique versus the whole lung in acquiring clinical relevant data (i.e. hyperinflated, normally, poorly and not inflated lung zones).
Thirty-four intubated sedated paralyzed patients with ALI/ARDS (mean age 56.2 ± 18.2 years, BMI 23.7 ± 3.6 kg/m$^2$, PEEP 11.2 ± 2.8 cm$H_2O$, $PaO_2/FiO_2$ 195 ± 81) were enrolled. Spiral CT scan of the lung was acquired at 120 kV and 250 mA during an end expiratory pause at 5 and 15 cm$H_2O$ PEEP. The lung CT regions of interest were manually delineated on each image by dedicated software (Maluna; University of Maanheim, Germany). The three CT lung sections were selected at the apex, hilum and base.
The Bland–Altman analysis showed a bias of 0.001% with an interval limits for agreement of 7.2% at 5 cm$H_2O$ PEEP and of 0.00001% with 98% at 15 cm$H_2O$ PEEP.
These data showed that the three CT scan technique provides an adequate measure of the distribution of lung compartments while strongly reducing X-ray exposure.

**Table 1**

| | PEEP 5 | | PEEP 15 | |
|---|---|---|---|---|
| Inflation | Whole lung | Three sections | Whole lung | Three sections |
| Hyper (%) | 0.04 ± 0.1 | 0.05 ± 0.1 | 1.1 ± 0.1 | 1.2 ± 0.1 |
| Normal (%) | 26.5 ± 0.1 | 26.3 ± 0.1 | 38.7 ± 0.1 | 37.6 ± 0.1 |
| Poor (%) | 33.2 ± 0.1 | 33.6 ± 0.2 | 31.3 ± 0.1 | 31.6 ± 0.1 |
| Not (%) | 39.7 ± 0.2 | 40.0 ± 0.1 | 28.5 ± 0.1 | 29.6 ± 0.1 |

### Reference

1. Picano E: *Br Med J* 2004, **329:**849-851.

## P112

### Beneficial effects of CT scan guided protective ventilation: multislice thoracic CT analysis

**G De Matos[1], J Borges[2], F Stanzani[1], V Okamoto[2], M Bueno[1], M Rodrigues[1], C Hoelz[1], R Albaladejo[1], M Fontana[1], R Caserta[1], D Santos[1], M Amato[2], C Barbas[1]**
*[1]Hospital Israelita Albert Einstein, Sao Paulo, Brazil; [2]University of São Paulo Medical School, São Paulo, Brazil*
*Critical Care* 2005, **9(Suppl 1):**P112 (DOI 10.1186/cc3175)

**Introduction** Recruitment maneuvers (RM) to open the lungs and PEEP titration to keep the lungs opened are believed to be an important component of a lung protective strategy in ARDS. There are scarce data assessing the occurrence of tidal recruitment (TR) and the gas distribution throughout the lung parenchyma by thoracic CT scan before and after maximal recruitment.
**Objectives** To analyze the occurrence of TR before and after stepwise recruitment maneuver (SRM) and PEEP titration by thoracic CT scan. To analyze the effects of the proposed maneuver on gas distribution throughout the lung parenchyma.
**Methods** Ten ARDS patients under mechanical ventilation were transported to the CT room and sequences of CT scans at expiratory and inspiratory pauses were performed before and after a SRM. The SRM consisted of 2-min steps of tidal ventilation with a fixed delta pressure PCV = 15 cm$H_2O$ and progressive PEEP levels (10, 20, 25, 35, 45, 25, 20, 15, 10 cm$H_2O$), RR = 10, I:E 1:1, and $FiO_2$ 1.0. At equivalent PEEP levels, the amount of collapsed tissue as well as the difference of collapsed tissue between inspiration and expiration (TR) were compared (before versus after maximal SRM). The amount of air content (ml) at end expiration – functional residual capacity (FRC) – was calculated and compared before maximal recruitment at PEEP of 20 cm$H_2O$ and after maximal SRM at PEEP of 25 cm$H_2O$.
**Results** See Figs 1 and 2. The TR difference is statistically significant at PEEP 25 cm$H_2O$ (Wilcoxon $P < 0.015$). There was a significant decrease of gas at FRC at non-dependent regions (Wilcoxon $P < 0.008$) and a significant increment of gas at the most dependent region with PEEP 25 cm$H_2O$ after maximal recruitment (Wilcoxon $P < 0.008$).
**Conclusion** The TR decreased significantly only under PEEP of 25 cm$H_2O$ after the SRM ($P < 0.0003$), suggesting that the application of SRM might be effective when accompanied by

**Figure 1 (abstract P112)**

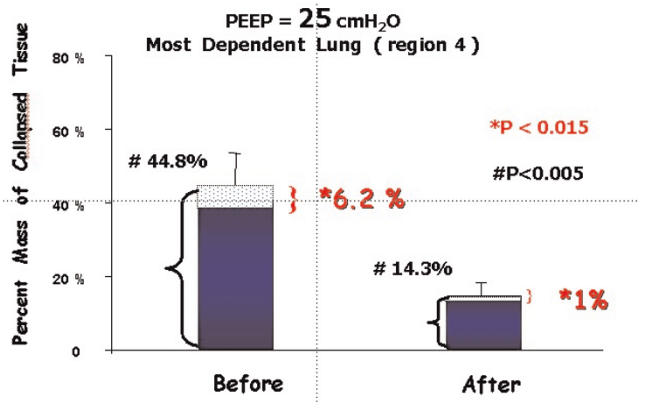
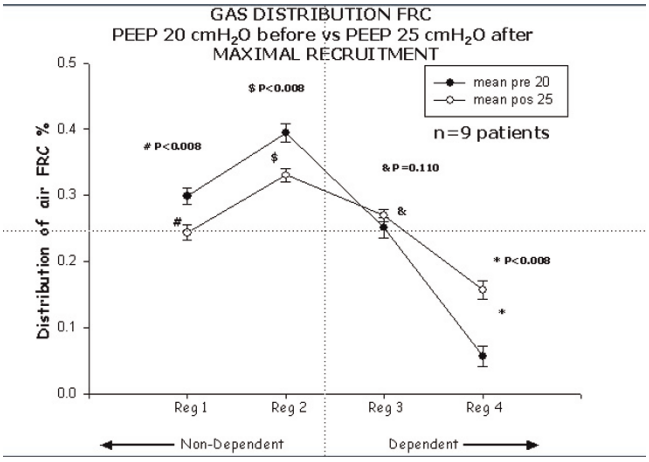



**Figure 2 (abstract P112)**




sufficient PEEP levels. Aeration of dependent portions of the lung after maximal SRM with maintenance of sufficient PEEP levels to keep the lungs opened (Wilcoxon $P < 0.008$) was associated with deflation of non-dependent regions, rendering the gas distribution more homogeneous.

## P113

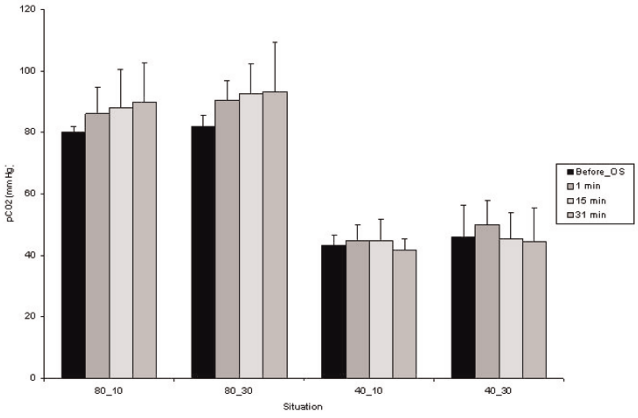
### Gas exchange impairment induced by open suctioning in ARDS: impact of permissive hypercapnia

**M Caramez, E Miyoshi, R Scott Harris, A Malhotra, R Kacmarek**
*Massachusetts General Hospital, Boston, MA, USA*
*Critical Care* 2005, **9(Suppl 1):**P113 (DOI 10.1186/cc3176)

**Background and aims** There is still controversy over the impact of open suctioning (OS) on gas exchange and the duration of suctioning. The goal of this physiologic study was to determine whether hypercarbia occurs following the use of OS in a lung lavage injured sheep and whether the level of baseline $PaCO_2$ and duration of suctioning impacts gas exchange.

**Methods** Six female sheep were lung injured by isotonic saline lavage until their $PaO_2$ dropped to 100 mmHg on an $FIO_2$ of 1.0,

**Figure 1 (abstract P113)**




Comparison of $PaCO_2$ between groups.

PEEP 5 $cmH_2O$ and VT 10 ml/kg. Then the VT was decreased to 6 ml/kg. RR was set to establish a $PaCO_2$ of 40 mmHg or 80 mmHg. OS was performed on each animal. $PaCO_2$ was randomly adjusted to 40 mmHg and 80 mmHg and the suction time randomly set at 10 s and 30 s. Before each of the four experimental conditions animals received recruitment maneuvers of 40 $cmH_2O$ CPAP for 40 s to establish a volume history, following by baseline for 15 min where $FiO_2$ and PEEP were set based on the ARDSnet $FiO_2$/PEEP [1]. OS was performed using a 14 Fr, TrachCare catheter at a pressure of −100 mmHg. Mean arterial blood pressure, heart rate, pulmonary and arterial wedge pressure, cardiac output, and arterial blood gases, were measured before, 1 min and then every 2 min after OS for 30 min.

**Results** During suctioning at 80 mmHg $PaCO_2$ at both 10 s and 30 s suctioning times, the $PaCO_2$ increased at 1, 15 and 31 min post suctioning ($P < 0.05$). $PaCO_2$ also increased at 1 min when the baseline $PaCO_2$ was 40 mmHg and the suction time was 30 s ($P < 0.05$) (Fig. 1). $PaO_2$ decreased 1 min post suctioning in all conditions but recovered by 15 min. Hemodynamics did not demonstrate any significance differences regardless of the experimental condition.

**Conclusions** OS causes in a significant increase in baseline $PaCO_2$ during baseline hypercapnia and when suctioning is applied for 30 s. OS regardless of conditions results in a decrease in $PaO_2$ that recovers rapidly post suctioning.

**Reference**

1. ARDS Network: *N Engl J Med* 2000, **342:**1301-1308.

## P114

### Rational airway control with high-frequency jet ventilation for percutaneous tracheostomy in patients with short fat neck

**R Badaev[1], M Croitoru[2], F Badaev[3], S Krimerman[2], U Teitelman[4], E Altman[4]**
*[1]Carmel Hospital, Haifa, Israel; [2]Bnai Zion Medical Center, Haifa, Israel; [3]City Hospital No 40, Ekaterinburg, Russia; [4]Rambam Hospital, Haifa, Israel*
*Critical Care* 2005, **9(Suppl 1):**P114 (DOI 10.1186/cc3177)

**Background and goal** Percutaneous tracheostomy (PCT) is a well-established bedside procedure for critically ill patients (CIP). Several techniques of airway control and ventilation during PCT have been suggested. Standard mechanical ventilation (SMV)

through an endotracheal tube (ETT) is widely used. Short fat neck (SFN) is considered a relative contraindication for PCT, mainly because of the possibility for airway complications during the procedure: loss of airway control, massive air leak, and sudden desaturation. We decided to examine our experience of airway control and ventilation by SMV and by high-frequency jet ventilation (HFJV) during PCT in the CIP with SFN and to determine which is more effective and reliable.

**Materials and methods** From January 1998 to June 2000, a group of 23 CIP with SFN underwent PCT by the Griggs technique and SMV, and from July 2000 to November 2001 a group of 25 patients underwent PCT by the same technique but with HFJV. One trained team performed all the bedside PCT under general anesthesia (GA). In the HFJV group, a Cook catheter was inserted through the existing ETT into the upper part of trachea and HFJV was initiated by the special ventilator AMS-1000 ACUTRONIC with the following parameters: $FiO_2 = 0.8–1.0$, Vt = 160–200 $cm^3$, I/E ratio = 0.5, respiratory rate = 100 bpm, driving pressure = 1.6–2.6 bar. Then the ETT was withdrawn from the trachea and larynx into the mouth along the ventilation catheter and PCT was performed. When PCT was finished the Cook catheter was removed together with the ETT. During PCT continuous routine monitoring and repeated blood gases were performed.

**Results** There was no significant statistically difference between the two groups in the sizes of the neck (mean 47.1 vs 47.3 cm, median 47 vs 47 cm, range 45–51 vs 47–53 cm, $P = 0.9$) and distance between the cricoid and sternal notch (mean 1.35 vs 1.37 cm, median 1.35 vs 1.5 cm, range 0.5–1.9 vs 0.5–1.9 cm, $P = 0.8$). Duration of the procedure for the two groups was identical: mean = 10.7 min, median = 11 min, range = 10–12 min. When SMV was used, only in 11 from 23 patients was it possible to create good conditions for performance of PCT. Impaling of the ETT and cuff rupture happened in one case, and displacement of the ETT into the pharynx took place in three cases (due to a short larynx). Moderate air leak from the larynx around the ETT accompanied almost every procedure. Additional egress of air from the tracheotomy site during the time of the dilation was the reason for pronounced desaturation in seven patients. On the contrary, PCT with HFJV passed smoothly: a small air leak from tracheotomy site during its dilation did not influence the level of oxygenation, only an increase in $PaCO_2$ values within acceptable limits was found. The difference between SMV and HFJV was statistically significant ($P < 0.001$).

**Conclusion** SMV cannot always supply the necessary conditions for PCT in patients with SFN and there are possibilities for development of serious complications. HFJV through a Cook catheter provides optimal conditions for manipulation on SFN, secures success of the procedure and prevents potential airway complications

## P115

### Comparison of two different percutaneous tracheostomy techniques with early and late complications in critically ill patients

**F Ugun, R Iscimen, N Kelebek Girgin, F Kasapoglu, H Coskun, F Kahveci**

*Uludag University Faculty of Medicine, Bursa, Turkey*

*Critical Care* 2005, **9(Suppl 1):**P115 (DOI 10.1186/cc3178)

**Background** Percutaneous tracheostomy (PT) is used in patients who receive long-term invasive mechanical ventilation. There are many different techniques in performing PT.

**Aim** The aim of this prospective study was to compare two different PT techniques with early and late complications in critically ill patients.

**Methods** After obtaining ethical committee approval, 60 adult patients were assigned randomly into two groups. Forceps dilatational PT and single-step dilatational PT were used in group F and group P, respectively. Heart rate, blood pressure and peripheral oxygen saturation, the level of tracheal entrance and number of punctions, major and minor complications and duration of the procedure were recorded during the procedure. Arterial blood samples were taken before the incision and after tracheostomy cannula was inserted, then pH, $pCO_2$, $pO_2$, $HCO_3$, BE, and $SaO_2$ were recorded. The endoscopic examinations of the cases were done during the procedure, at the decannulation time and 1 month after decannulation. The *t* test, Mann–Whitney U test, Wilcoxon signed rank test, chi-squared test and Kruskal–Wallis test were used for statistical analysis.

**Results** The demographic data, duration of intubation time and procedure time were similar in both groups. There were no significant differences in hemodynamic data between the groups. It was noticed that in both groups there was a decrease in pH ($P < 0.001$) and an increase in $pCO_2$ ($P < 0.01$). Tracheal ring damage that was one of the minor complications in Group P was significantly gretaer ($P < 0.05$). There were no significant differences in major complications between the groups. In Group F tracheal stenosis in one case and laryngotracheal separation in another case were detected with endoscopic examination.

**Conclusion** The present study demonstrated that single-step dilatational PT may be an alternative to forceps dilatational PT, but we conclude that to maintain a decrease in complications endoscopic visualisation could be used.

## P116

### Biomechanical experimental evaluation of percutaneous tracheostomy to compare the Ciaglia and Griggs techniques

**I Rozin[1], M Croitoru[2], E Radinsky[3], N Altman[3], U Teitelman[3], E Altman[3]**

*[1]Puria Hospital, Tveria, Israel; [2]BZMC, Haifa, Israel; [3]Rambam Hospital, Haifa, Israel*

*Critical Care* 2005, **9(Suppl 1):**P116 (DOI 10.1186/cc3179)

**Introduction** The aim of our study was to create a method for biomechanical experimental evaluation of the percutaneous tracheostomy (PCT) technique and perform its assessment in order to minimize possible trauma of cervical trachea inherent in this procedure. Nowadays two techniques of PCT, Ciaglia and Griggs, are employed.

Every technique is based on gradual tearing of the hole in the cervical trachea by specially designed dilators. We suggested that biomechanical study of the different stages of PCT will help to understand all these processes and to clarify the reasons for traumatic perioperative complications.

**Materials and methods** PCT by the Ciaglia technique ($n = 10$) and by the Griggs technique ($n = 10$) were performed on fresh dead pigs with body mass of 115 ± 3 kg. A Portex set of instruments was used for the Griggs technique and a Cook set of instruments for the Ciaglia technique. During PCT special measurements were performed with the help of an electronic dynamometer (MRC): piercing force applied on needle cannula, penetrating force applied on 14 F dilator, pulling force applied on branches of Griggs dilating forceps, pushing force applied on Ciaglia Blue Rhino dilator, pushing force applied on distal end of tracheostomy tube no. 8 with introducer (Portex set) and pushing force applied on distal end of tracheostomy tube no. 8 loaded on dilator (Cook set). On the base of these measurements calculation of energy spent for these stages of PCT was made. At the end of each experiment evaluation of cervical trachea was performed to

measure the size of tracheotomy performed by the Ciaglia and Griggs dilators.

**Results** Application of the Ciaglia dilator requested 1.54 times more energy than the Griggs dilator forceps ($P < 0.05$). Formation of tracheotomy by the Ciaglia dilator was more exact than by Griggs forceps due to special markings on the dilator. The work with Griggs dilating forceps requested more experience due to the absence of any markings on the dilator. The most dangerous moments of PCT for laceration of the cervical trachea were: dilation of hole in the cervical trachea in the Griggs technique and insertion of the tracheostomy tube loaded on the dilator in the Ciaglia technique. The macroscopic appearance and transverse diameter of tracheotomy performed by the Ciaglia and Griggs techniques were the same despite the different instruments used for dilation ($P < 0.05$)

**Conclusions** PCT by the Ciaglia and Griggs techniques has almost similar biomechanical characteristics. In spite of the difference in the design of dilators the final result of the two techniques is the same. Both of them have dangerous moments. In order to prevent laceration of the cervical trachea during PCT some improvements must be made in instrumentation.

## P117

### Does tracheostomy improve respiratory functions in mechanically ventilated patients

**F Pürnek Akin, L Dösemeci, M Cengiz, M Yilmaz, A Ramazanoglu**
*Akdeniz University Faculty of Medicine, Antalya, Turkey*
*Critical Care* 2005, **9(Suppl 1):**P117 (DOI 10.1186/cc3180)

**Objectives** Tracheostomy has been widely performed in the intensive care unit and has many advantages when compared with translaryngeal intubation. Our hypothesis was that tracheostomy would also result in improved pulmonary function through changes in respiratory mechanics and tracheabronchial touilette.

**Study design** A prospective, observational, clinical study. A before-and-after trial of 65 patients undergoing tracheostomy.

**Patients and methods** A consecutive group of critically ill patients requiring prolonged mechanical ventilation was included in the study (15 July 2004–1 December 2004). Percutaneous tracheostomy was performed using the dilatational forceps technique described by Griggs. Respiratory mechanics (ventilator settings, airway pressures) and arterial blood gases ($PaO_2$, $PaCO_2$, pH) were measured before and after tracheostomy (at 24, 48 and 72 hours) in 65 patients. Calculated variables included minute ventilation, dynamic and static compliances and $PaO_2$:$FiO_2$ ratio (Harowitz).

**Results** A total of 65 patients (with a mean age of 50.6 ± 20 years) underwent tracheostomy a mean of 5 ± 2.6 days after admission. The Glasgow Coma Scale score and Acute Physiology and Chronic Health Evaluation II score were 8.3 ± 3.7 and 20.61 ± 5.3, respectively. We could not find statistically significant differences in respiratory mechanics, blood gases and pH after tracheostomy when we considered all of the patients. Then, we evaluated the results by dividing the patients into two groups according to the Harowitz ratio. Forty-three patients had Harowitz ratio greater than 250 (396.5 ± 105.5) and 22 patients less than 250 (201.1 ± 36.5). Both groups were analyzed with repeated-measures analysis of variance and we found that the Harowitz ratio at 24 hours (265.3 ± 71), 48 hours (269 ± 26) and 72 hours (274 ± 93) improved significantly after tracheostomy individually ($P = 0.002$, $P = 0.018$, $P = 0.004$, respectively) in the patients with a Harowitz ratio less than 250.

**Conclusion** Our study showed that percutaneous tracheostomy improves the $PaO_2$:$FiO_2$ (Harowitz) ratio in the mechanically ventilated patients who had Harowitz ratio less than 250 before tracheostomy, but does not improve it in the patients with Harowitz ratio greater than 250.

## P118

### Routine chest radiography following percutaneous dilatational tracheostomy

**M Hughes, L Clark, G Dempsey**
*University Hospital Aintree, Liverpool, UK*
*Critical Care* 2005, **9(Suppl 1):**P118 (DOI 10.1186/cc3181)

**Background and goal** The role of routine chest radiography (CXR) following percutaneous dilatational tracheostomy (PDT) has recently been questioned [1].

**Materials and methods** We have performed a prospective observational study, on a mixed medical–surgical critical care unit, on 110 patients undergoing PDT under bronchoscopic guidance to assess the utility of routine postoperative chest radiography. Data were collected on all patients undergoing PDT from 1 November 2003–14 December 2004. Two post-procedure CXRs were reviewed and compared with those taken prior to PDT. Significant findings were barotrauma (pneumothorax, pneumomediastinum) and consolidation not noted on the pre-procedure film. Post-procedural films reviewed were those taken immediately after PDT and, to exclude the possibility of overlooking evidence of minor barotrauma, one further film taken between 24 and 96 hours.

**Results and observations** One hundred and ten patients underwent PDT; 83 (75%) were uncomplicated. Complications were recorded in 27 (25%) patients. These included multiple attempts at needle insertion (> 2), bleeding (> 3 soaked gauze swabs), tracheal ring fracture, posterior tracheal wall injury, and malplacement. Ninety-five (86%) patients had two post-procedural CXRs reviewed. Fourteen (13%) patients had at least one CXR reviewed after PDT. One patient had no CXR after PDT. New abnormalities were noted on three (3%) post-procedure CXRs. No new pneumothoraces were seen. Patients having uncomplicated PDTs had no new CXR changes (Table 1).

**Table 1**

| PDT complicated? | Number of CXRs reviewed | New problem on CXR |
|---|---|---|
| NO, $n = 71$ (65%) | 2 | 0 (0%) |
| YES, $n = 24$ (22%) | 2 | 3 (13%) |
| NO, $n = 11$ (10%) | 1 | 0 (0%) |
| YES, $n = 3$ (3%) | 1 | 0 (0%) |

PDT, percutaneous dilatational tracheostomy; CXR, routine chest radiography.

**Conclusions** Routine CXR following uncomplicated PDT performed under bronchoscopic guidance is not warranted. Concern that evidence of minor barotrauma may be missed on the early post-procedural film is not bourne out by review of the film taken 24–96 hours after the event. The role of CXR following PDT appears to be restricted to those patients undergoing complicated procedures. This will lead to reductions in both medical costs [2] and exposure of staff and patients to ionising radiation.

**References**

1. Datta D, Onyirimba F, McNamee MJ: *Chest* 2003, **123:**1603-1606.
2. Tarnoff M, Moncure M, Jones F, *et al.*: *Chest* 1998, **113:**1647-1649.

**P119**

## Consequences of adverse events with handling of the orotracheal cannula in intensive care unit

**S Silva[1], K Padilha[2]**
*[1]Sírio Libanês Hospital, São Paulo, Brazil; [2]University of São Paulo, Brazil*
*Critical Care* 2005, **9(Suppl 1):**P119 (DOI 10.1186/cc3182)

**Objectives** To identify the adverse events regarding handling of the orotracheal cannula in the ICU and to evaluate its impact on the patient's severity and on the nursing workload.
**Method** Data were prospectively collected during a 3-month period, in two general ICUs of a hospital in the city of São Paulo, Brazil, using a file card to record the occurrences. Patient's severity and nursing workload were evaluated 24 hours before and 24 hours after the occurrence of the event, respectively, by means of the Simplified Acute Physiology Score (SAPS II) and the Therapeutic Intervention Scoring System-28 (TISS-28).
**Results** In the period of the study 212 patients were admitted, 47 (22%) of which were victims of 80 adverse events during the their stay at the ICU. There was a total of 19 (24.0%) adverse events regarding handling of the orotracheal cannula. Of these were observed 14 (73.0%) not programmed withdrawals of the orotracheal cannula, three (16%) blockages of the cannula for secretion corks and two (11%) cuffs emptied. A statistically significant difference was found both in the SAPS II ($P < 0.042$) and TISS-28 ($P < 0.001$), evidenced before and after the event. One verified reduction of the patient's severity, but an increase on the nursing workload as a consequence of these events.
**Conclusions** The results of this investigation reinforce the need for investments to qualify professionals to work with critical patients as a major measurement for safety nursing assistance and quality in the ICU.

**P120**

## A prospective study comparing standard laryngoscopy with the trachview videoscope system for orotracheal intubation

**L Roppolo, P Pepe, J Martinez**
*University of Texas Southwestern Medical Center and the Parkland Health and Hospital System, Dallas, TX, USA*
*Critical Care* 2005, **9(Suppl 1):**P120 (DOI 10.1186/cc3183)

**Background** As a technology to facilitate a difficult endotracheal intubation (ETI), the TrachView Videoscope (TrVV) consists of a narrow high-resolution fiberoptic cable whose tip is positioned at the distal end of the endotracheal tube. The image is displayed on a small portable bedside monitor.
**Objective** To determine the reported ease of use of the TrVV and the accompanying percent improvement in assessment of the glottic opening (POGO) score when operated by individuals of varied levels of ETI experience.
**Methods** The study was conducted in two phases using a mannequin model during an airway workshop for first-year, second-year and third-year (R1, R2, R3) emergency medicine (EM) residents with ETI experience and first-year and second-year medical students with no ETI experience. In phase 1, after a 10-min demonstration of the TrVV, EM residents assessed the POGO score using direct laryngoscopy (DL) and sequentially compared it with their observed POGO score using the TrVV. Phase 2 consisted of a crossover study with the medical students who were randomized into two groups: a group first instructed in DL and a second first instructed in TrVV. The students were given a 10-min demonstration of each technique and had two opportunities to return the demonstration. The POGO scores noted by the students were then recorded for each technique. The groups were then crossed and the process was repeated. Additional information collected from study subjects included reported ease of use of the TrVV and improvement in ETI success.
**Results** In Phase 1, the overall median POGO score for DL was 50%, and the median POGO score for TrVV was 100% ($P < 0.001$). The median differences in POGO scores (TV – DL) were: 50% for R1s ($n = 4$), 50% for R2s ($n = 10$), and 25% for R3s ($n = 11$). Of these, 86% ($n = 24$) reported that the TrVV was 'easy' to use and 11% ($n = 3$) were undecided. Only one reported it to be 'difficult' to use. Most (82%; $n = 23$) reported that the TrVV improved their ETI attempt, but 14% ($n = 4$) reported no difference. In Phase 2, the overall median TrVV and DL POGO scores ($n = 34$) were 75% and 25%, respectively ($P = 0.004$). The median difference in POGO scores (TV – DL) for the two groups were: 75% for Group 1 (DL first) and 50% for Group 2 (TrVV). Of all participants, 68% ($n = 25$) ranked the TrVV as 'easy', 22% ($n = 8$) were undecided, and 11% ($n = 4$) ranked the TrVV as 'difficult' to use. Meanwhile, 57% ($n = 21$) reported that it improved their ETI attempts, 27% ($n = 10$) reported no difference, and 11% ($n = 4$) reported 'more difficulty'.
**Conclusion** The Trachview Videoscope can significantly improve the POGO score assessment over direct laryngoscopy and, in the laboratory setting, most operators report it to be an easy to use technique that improves their intubation success, regardless of level of experience.

**P121**

## Treatment of post-intubation tracheal stenosis with the Nd-YAG laser at the NRITLD

**S Arami[1], H Jabbardarjani[1], M Masjedi[2]**
*[1]NRITLD, London, UK; [2]NRITLD, Tehran, Iran*
*Critical Care* 2005, **9(Suppl 1):**P121 (DOI 10.1186/cc3184)

**Background and objective** Tracheal intubation is a common procedure for critically ill patients and may lead to local complications such as tracheal destruction and post-intubation stenosis. Utilization of the Nd-YAG laser can correct intraluminal airway lesions including webs, granulation tissues and fibrous bands. It decreases the hospitalization period, complications and expenses and also saves the medical staff's time and energy.
**Materials and methods** An uncontrolled clinical trial was performed in post-intubation tracheal stenosis cases admitted to the NRITLD between 1994 and 1999. Based on bronchoscopic findings, patients with the following inclusion criteria underwent laser therapy: length of stenosis less than 2 cm, tracheal lumen diameter more than 5 mm and lesions with granulation tissue type. Others candidated for surgery. Laser therapy was carried out by fiberoptic bronchoscopy under local anesthesia. For those patients with tracheal lumen diameter between 5 and 10 mm rigid bronchoscopy was performed under general anesthesia.
**Results** Of the total 32 patients, 25 met the primary criteria for laser therapy, from which 22 (88%) were completely cured. Because of poor general condition, five of seven other patients who had been referred for surgery also underwent laser therapy; therefore, a total of 30 patients (93%) took advantage of this technique. Overall, 23 patients were treated only with a laser, two patients only with surgery and seven patients with a combination of these two approaches.
**Conclusions** This trial revealed that if patients with post-intubation tracheal stenosis are selected correctly, laser therapy could be used as a beneficial and safe method with satisfactory results.

## P122

### Weaning from mechanical ventilation using assisted spontaneous breathing plus CPAP versus assisted spontaneous ventilation: our experience

**M Di Nardo, A Tomagnini, P Cosimini, F Forfori, L Roventini, F Giunta**
*University of Pisa, IV ICU, Department of Anesthesiology and Intensive Care, Pisa, Italy*
*Critical Care* 2005, **9(Suppl 1):**P122 (DOI 10.1186/cc3185)

**Introduction** In this retrospective study, we evaluated two different modes of weaning: assisted spontaneous breathing (ASB) plus CPAP with automatic tube compensation (Evita 4, Draeger Medical, Germany) versus assisted spontaneous ventilation (ASV) (Galileo Gold, Hamilton Medical, Switzerland) in 80 patients who had undergone abdominal surgery. Our target was to assess differences in weaning times using different modes of assistance.
**Methods** Forty patients were enrolled in two groups of weaning: group A was treated with ASB and CPAP, and group B was treated with ASV. Both groups after mechanical support underwent a 2-hour T-tube ventilation before extubation and were sedated with remifentanil beginning from 6 μg/kg/hour and titrated to reach the Ramsay sedation scale 3–4 without the help of other drugs; supplemental midazolam bolus was administered if the patients were still agitated. The time of weaning and other events during ASB or ASV (discomfort during ventilation, bad-adaptation) were recorded in each patient.
**Results** We did not find a great statistical difference among the two groups (20 ± 10.75 vs 21.6 ± 8.46, $P = 0.3$). We had three cases of weaning failure with ASB and CPAP and five with ASV after 30–36 hours from extubation. If the ventilator setting was done following the patient requests, few signs of discomfort were found (agitation, tachycardia, hypertension, etc.) and a good patient–ventilator interaction can be granted using both methods of ventilatory support.
**Conclusion** We did not find any statistical difference in the two groups: times for weaning were almost the same. Our data cannot suggest the use of a specific modality of weaning, because the number of patients in the study is too small. But both ways of assistance were well tolerated by the patients.

## P123

### Intraoperative monitoring of pHi as a predictor of successful extubation at the end of major abdominal operations

**P Drimousis, K Stamou, A Koutras, C Cristoloveanou, F Archodovassilis, A Kapralou, D Theodorou, S Katsaragakis**
*Hippocratio Hospital, Athens, Greece*
*Critical Care* 2005, **9(Suppl 1):**P123 (DOI 10.1186/cc3186)

**Introduction** Reintubation following failed extubation is an independent predictor of prolonged ICU stay, morbidity and mortality. Extubation criteria at the end of surgical procedures are similar to those applied to critically ill patients in mechanical ventilation.
**Patients and methods** This prospective, observational, non-interventional study was conducted in a teaching University Surgical Clinic. Data from all consecutive patients that underwent elective major abdominal operations by a single surgeon in a 6-month period were recorded and examined. In all patients, 30 min prior to the induction of anesthesia, a nasogastric tonometry catheter was inserted and measurements were obtained by a tonometer. At the end of the operation, the optimal goal was successful extubation unless prevented by the patient's general condition. Patients were extubated when they complied with the following criteria: patient alert and rested, arterial pH > 7.25, $PO_2$ > 60 mmHg with $FiO_2$ < 50% and positive end expiratory pressure (PEEP) < 5 $cmH_2O$, $PCO_2$ < 50 mmHg, tidal volume > 5 ml/kg, respiratory rate < 24/min, negative inspiratory force more than −20 $cmH_2O$, minute ventilation <10 l/min, stable hemodynamic status, hemoglobin >10 mg/dl, presence of cough and no excessive or thick secretions. Extubation failure was defined as the need for reintubation within 24 hours.
**Results** Twenty-four consecutive patients (11 males, 13 females) of mean age of 66.79 years (range: 27–85), who underwent elective major abdominal operations, were included in the study. Mean operative time was 3.16 hours (range: 1.8–4.5). Patients were divided into two groups based on extubation outcome. Twenty-two of the patients met the extubation criteria at the end of the procedure and were therefore extubated. Three of these patients required reintubation within the next hour due to acute respiratory failure. One patient was not extubated due to acidosis (arterial pH < 7.25, hypothermia: 35.5°C) and one other patient was not extubated as his hemoglobin level had dropped to 8 mg/dl. Consequently, 19 patients that were successfully extubated were included in group I and five patients were included in group II.
Mean values of baseline measurements for pHi in the two groups were similar ($P = 0.773$). In all patients, the mean pHi value at induction of anesthesia compared with the means of 30-min and 60-min measurements differed significantly ($P < 0.001$). pHi values decreased for the first 2 hours of operating time in a linear pattern. Thereafter, pHi values appeared stable. No further decrease was observed until the end of the operation. The mean pHi values at the end of the operation between the two groups differed significantly ($P = 0.027$, confidence interval: −6.175 to −0.408).
**Conclusion** Early detection of extubation failure in the operative room will save time and will orient resuscitation efforts towards more beneficial actions for the patient (hypothermia prevention, volume depletion, hemodynamic stability).

## P124

### Low f/Vt ratio is associated with successful extubation in our pulmonary patients

**T Subic, I Drinovec, F Sifrer**
*Clinical Hospital Golnik, Slovenia*
*Critical Care* 2005, **9(Suppl 1):**P124 (DOI 10.1186/cc3187)

**Background** Weaning from mechanical ventilation is usually conducted in an empirical manner and a standardized approach has not been developed. A variety of criteria have been proposed as predictors of the success or failure of weaning attempts, among them rapid shallow breathing – the ratio of respiratory frequency to tidal volume (f/Vt).
**Aims** The aim of the study was to evaluate whether low f/Vt ratio (< 105) is associated with successful extubation in our pulmonary patients. We also wanted to find out whether there is a correlation between low f/Vt ratio and our previous criteria: stable clinical state, maximal inspiratory pressure > 25 $cmH_2O$, vital capacity >1000 ml, respiratory frequency < 35/min and also arterial blood gas analysis.
**Methods** A prospective trial was conducted in 37 patients receiving mechanical ventilation for more than 24 hours because of acute respiratory failure in our intensive care unit because of pulmonary disease: pneumonia (15 patients), chronic obstructive pulmonary disease (nine patients), asthma (four patients), bronchiectasis (four patients), fibrothorax (four patients), pyopneumothorax (one patient). When patients were able to breathe spontaneously we measured the respiratory frequency (f), tidal volume (Vt), maximal inspiratory pressure (MIP), vital capacity

(VC), minute ventilation (MV), $PaCO_2$, $PaO_2$ and calculated the f/Vt. We measured criteria many times in each patient until extubation.
Criteria for extubation were a stable clinical state of patient and all three or at least two of three criteria: MIP > 25 $cmH_2O$, VC >1000 ml and/or f < 35/min. Successful extubation was determined as spontaneous breathing for at least 72 hours after extubation.
**Results** Data from 37 patients were obtained (51% women, age 30–84 years). Median duration of mechanical ventilation was 13 days, range 2–30 days. Thirty patients (30/37, 82%) were extubated, all had ratio f/Vt less than 105. Among them 28 patients (28/30, 93%) underwent successful extubation, two patients (2/30, 7%) were reintubated because of laryngeal edema. Seven patients (7/37, 18%) were not extubated, all of them had high f/Vt ratio (>105). There was positive correlation between f/Vt and respiratory frequency, and negative correlation between f/Vt and vital capacity and between f/Vt and maximal inspiratory pressure. No correlation was found between f/Vt ratio and $PaCO_2$ ($P = 0.7$), $PaO_2$ ($P = 0.7$), $FiO_2$ ($P = 0.4$).
**Conclusions** Low f/Vt ratio (<105) was associated with successful extubation in our pulmonary patients. There was good correlation between low f/Vt ratio and maximal inspiratory pressure, vital capacity and respiratory frequency. There was no correlation between f/Vt ratio and $PaCO_2$ and $PaO_2$ – blood gas analysis only should not be a criterion for extubation.

### P125

### Weaning patients with high cardiac output state: influence on central venous pressure and right ventricular stroke work index

**P Marcelino[1], D Sargento[1], N Germano[1], S Marum[1], A Fernandes[1], J Ribeiro[1], M Lopes[2]**
*[1]Hospital Curry Cabral, Lisbon, Portugal; [2]Faculty of Medicine, University of Lisbon, Portugal*
*Critical Care* 2005, **9(Suppl 1):**P125 (DOI 10.1186/cc3188)

**Objective** The authors studied the changes in several haemodynamic parameters during a weaning trial of a cohort of post-liver transplant patients with a high cardiac output (CO).
**Design and setting** An observational, prospective study at a 14-bed medical/surgical ICU.
**Materials and methods** Twenty-five patients were enrolled; all presented cardiac index > 4 l/min/$m^2$. The following parameters were evaluated: heart rate (HR), mean arterial pressure, central venous pressure (CVP), pulmonary capillary wedge pressure (Pw), CO, systolic pulmonary artery pressure (SPAP) and diastolic pulmonary artery pressure (DPAP), systemic vascular resistance index (SVRI), pulmonary vascular resistance index (PVRI), left ventricular stroke work index (LVSWI) and right ventricular stroke work index (RVSWI). The determinations were performed before disconnection from mechanical ventilation, 30 min after disconnection and 4–6 hours after disconnection.
**Results** CVP decreased significantly after disconnection (–24% at 30 min and –20% at 4–6 hours), the CO remained unchanged, inducing a marked and progressive increase in RVSWI. The remaining parameters changed insignificantly. All patients were successfully weaned from mechanical ventilation. The variation of the parameters evaluated is presented in Table 1, with mean values and standard deviation.
**Conclusions** The weaning from mechanical ventilation in patients with high CO, particularly post-liver transplant patients, induces a significant increase in RVSWI, and a decrease in CVP. From the data presented, the clinical impact of this observation is not clear.

**Table 1**

| Parameter | Ventilated | 30 min post-discharge | 4–6 hours post-discharge |
|---|---|---|---|
| MBP (mmHg) | 96.8 ± 10.2 | 97.1 ± 9.8 | 97.3 ± 9.9 |
| MPAP (mmHg) | 24.3 ± 3 | 23.6 ± 2.8 | 26 ± 3.2 |
| HR (bpm) | 97.6 ± 8.1 | 100.4 ± 9.2 | 75.5 ± 10.1 |
| Pw (mmHg) | 12.4 ± 3.9 | 13.4 ± 4 | 13.6 ± 3.8 |
| CVP (mmHg) | 12.6 ± 4.4 | 9 ± 3.1 | 9.9 ± 3.3 |
| CI (l/min/$m^2$) | 4.9 ± 0.71 | 5.3 ± 0.82 | 5 ± 0.78 |
| LVSWI (g $m/m^2$) | 57.8 ± 5.5 | 60.5 ± 8.2 | 57.9 ± 6.1 |
| RVSWI (g $m/m^2$) | 8.1 ± 1.7 | 10.6 ± 1.5 | 12.3 ± 1.6 |
| SVRI (dynes s) | 1378 ± 190 | 1334 ± 202 | 1396 ± 197 |
| PVRI (dynes s) | 195 ± 21 | 158 ± 20 | 193 ± 17 |

MBP, mean blood pressure; CI, cardiac index.

### P126

### Predicting success in weaning from mechanical ventilation: preliminary results from a multicentric study

**S Vieira[1], C Teixeira[2], L Nasi[1], R Oliveira[3], C Trevisan[1], A Savi[2], R Wickert[2], R Cremonesi[2]**
*[1]Clinicas Hospital, Porto Alegre, Brazil; [2]Moinhos de Vento Hospital, Porto Alegre, Brazil; [3]Santa Casa Hospital, Porto Alegre, Brazil*
*Critical Care* 2005, **9(Suppl 1):**P126 (DOI 10.1186/cc3189)

**Introduction** Failure in weaning from mechanical ventilation (MV) occurs in up to 25–30% of patients, being associated with high mortality. Indexes predicting success can be very helpful clinically. However, their predictive capacity is sometimes low and there are controversies concerning which ones have to be used.
**Objective** To evaluate weaning predictor indexes in a group of patients during weaning from MV.
**Methods** Patients under MV for at least 48 hours, submitted to a spontaneous breathing trial (SBT) during 30 min, extubated according to the clinical assistant physician's decision and followed for 48 hours, were included. They were evaluated concerning age, sex, APACHE score, Glasgow score, causes of ICU admission and mechanical ventilation, length of hospital and ICU stay, time of mechanical ventilation, drugs used and clinical characteristics. At the first and 30th minutes from SBT were analyzed: arterial blood gases, hemodynamic parameters as arterial blood pressure and cardiac rate, respiratory parameters as respiratory rate (RR), tidal volume, rapid shallow breathing index (f/VT), maximal inspiratory (PImax) and expiratory (PEmax) pressures. Comparisons were made between two groups of patients: success versus failure, defining failure as return to mechanical ventilation in the first 48 hours.
**Results** Two hundred and one patients were studied. Overall mortality rate was 16%. Return to mechanical ventilation occurred in 32%. The most important differences comparing success with failure groups were: lower mortality rate (12% versus 27%, $P < 0.01$), shorter length of hospital and ICU stay (27 ± 21 versus 35 ± 21 days, $P < 0.001$ and 13 ± 12 versus 19 ± 14 days, $P < 0.001$); less incidence of dyspnea (37% versus 58%, $P < 0.001$), higher $PaO_2$ at 30 min (100 ± 30 versus 88 ± 25 mmHg, $P < 0.001$), lower RR at the first and 30th minutes (24 ± 6 versus 28 ± 7 bpm, $P < 0.001$, and 24 ± 6 versus 30 ± 8 bpm, $P < 0.001$), lower f/VT at first and 30th minutes (58 ± 31 versus 78 ± 45, $P < 0.01$ and 56 ± 38 versus 98 ± 74, $P < 0.001$), and higher PImax at 30 min (42 ± 15 versus 36 ± 14 cmH2O, $P < 0.05$).
**Conclusions** In this group of patients a great number failed in the weaning process showing, as expected, a higher mortality rate. Parameters related to failure were longer length of hospital and

ICU stay, higher incidence of dyspnea, higher respiratory rate and f/VT index both at the beginning and at the end of the trial, and lower level of oxygenation and lower PImax at the end of the trial.

**Acknowledgements** Other members from the Weaning Research Group: CE Hahn, ES Oliveira, FC Alves, F Callefe, JB Hervé, KB Pinto, K Hartmann, L Cassel, LG Borges, MB Blom, P Pinheiro, R Zancanaro, SFM Brodt, TF Tonietto, J Horer, NB Silva.

## P127

## Weaning of mechanical ventilation in the intensive care units of Brazil

**M Damasceno[1], C David[1], P Souza[2], P Mello[3], J Valiatti[4], A Gut[5], J Amaral[6], S Group of Mechanical Ventilation[7]**
*[1]UFRJ, Rio de Janeiro, Brazil; [2]Hospital de Clínicas de Niterói, Brazil; [3]Hospital São Marcos, Teresina, Brazil; [4]Hospital Padre Albino, Catanduva, Brazil; [5]HC FMB, Botucatu, Brazil; [6]Hospital São Paulo, Brazil; [7]AMIB, São Paulo, Brazil*
*Critical Care* 2005, **9(Suppl 1):**P127 (DOI 10.1186/cc3190)

**Introduction** The discontinuation of mechanical ventilation represents an important stage for patients in mechanical ventilation in the ICU, and knowing how this procedure is being managed make us better intensivist physicians. Our purpose in this study was to determine some aspects of the patients that were being weaned from mechanical ventilation in Brazil.

**Methods** A study of 1 day prevalence was done in 34 ICUs of Brazil. In the questionaire answered by the ICUs, we present here the modes of ventilation used in the weaning stage, the diseases that were the reason for the indication of mechanical ventilation, and some aspects about the patients with ventilator-associated pneumonia (VAP).

**Results** The study evaluated 390 patients, with 215 patients being in some kind of ventilatory support. Sixty-nine patients (69/215) were in discontinuation of mechanical ventilation. The patients were distributed as: PSV, 48 (48/69); SIMV + PSV, nine (9/69); spontaneous, four (4/69); SIMV, three (3/69); PCV, three (3/69); and VCV, two (2/69). The causes of admission in mechanical ventilation of this group were COPD (1/69), neuromuscular disease (2/69), coma (9/69), and acute respiratory failure (57/69). On the day of the study, 38 patients were with pneumonia (38/69): 20 were with VAP, 11 were with nosocomial pneumonia and seven were with community pneumonia. The medium times of mechanical ventilation were, respectively, 39.2 days, 23.7 days and 8.3 days.

**Conclusion** About 32% of the patients in mechanical ventilation were being discontinued. PSV was the principal mode used, while acute respiratory failure was the main cause of mechanical ventilation's use. The incidence of VAP was 29%, and it was related with the long median time of mechanical ventilation.

## P128

## Chest physiotherapy is effective in the management of intensive care unit patients immediately after extubation

**ES Papadopoulos, TH Kyprianou, S Nanas**
*Critical Care Department, Medical School, National and Kapodistrian University, Evangelismos Hospital, Athens, Greece*
*Critical Care* 2005, **9(Suppl 1):**P128 (DOI 10.1186/cc3191)

**Introduction** Physiotherapists are routinely involved in the management of patients in ICUs. Despite the necessity of physiotherapists in the ICU, little scientific evidence exists as to the therapeutic efficacy of their intervention. Physiotherapists are often involved in the weaning process, in order to assist patients to maintain a good respiratory function and prevent reintubation. Preliminary results showed that the respiratory function was significantly improved with chest physiotherapy immediately after extubation [1]. No other studies have been carried out so far to support or reject the role of physiotherapists in the weaning process.

The aim of this study is to investigate the short-term effect of chest physiotherapy versus no physiotherapy following extubation, in order to provide further scientific insight of its role in this area.

**Patients and methods** Twenty-four ICU patients with various diagnoses were entered into the study as soon as they were extubated. Profusely confused patients were excluded. Patients eligible for the study were randomly allocated to two groups. The first group ($n = 12$) was the experimental group where patients received chest physiotherapy (upper and lower limb active exercises, deep breathing exercises, chest percussion and vibrations, huffing and assisted cough), and the second group (control, $n = 12$) received instructions but no physiotherapy. Outcome measures, which are described in Table 1, took place immediately after extubation in both groups followed by chest physiotherapy only in the experimental group. Following treatment, patients in both groups were allowed to rest for 30 min and all measurements were repeated in order to detect differences.

**Results** Wilkoxon rank tests revealed significant differences between the two groups (Table 1). Specifically, patients in the experimental group had significantly improved vital capacity ($P < 0.05$) and Pimax ($P < 0.05$) following chest physiotherapy. No significant differences were noted in any of the other outcome measures. Furthermore, within-group comparisons revealed that patients in the experimental group had significantly increased VC ($P < 0.01$) and Pimax ($P < 0.01$) immediately after physiotherapy whereas no significant improvement was noted within the control group.

**Table 1**

| Measurement | Physiotherapy group | Control group | *t* test |
|---|---|---|---|
| pH | 7.4 ± 0.03 | 7.3 ± 0.01 | Not significant |
| $PO_2$ | 96.4 ± 33 | 100.13 ± 40 | Not significant |
| $PCO_2$ | 41.6 ± 9.4 | 48.9 ± 14 | Not significant |
| $SaO_2$ | 96.2 ± 3 | 91.9 ± 0.1 | Not significant |
| Pimax | −66 ± 33 | −41 ± 23 | $P < 0.05$ |
| VC | 1501 ± 536 | 997 ± 459 | $P < 0.05$ |

**Conclusion and discussion** The results of the present study revealed that standard chest physiotherapy resulted in significant improvement of both the vital capacity and the maximum negative inspiratory pressure in ICU patients immediately after extubation. Despite the small number of patients, the presence of a control group to count for time and learning effect indicate that chest physiotherapy may have an important role in the success of weaning. Future controlled studies with more patients and additional outcome measures and categorization according to diagnosis are necessary in order to further establish an evidence-based physiotherapy practice in this area.

**Reference**

1. Papadopoulos M, Kyprianou T, Nanas SN, Routsi C, Roussos C: **Chest physiotherapy after extubation affects vital capacity and inspiratory muscles strength.** *Intensive Care Med* 2002, **28 (suppl 1):**S198.

## P129

### Can high efficiency aerosol delivery continue after extubation?

**J Fink[1], P Dunne[2], R MacLoughlin[2], G O'Sullivan[2]**
*[1]Aerogen, Inc, Mountain View, CA, USA; [2]Aerogen, Ireland, Ltd, Galway, Ireland*
*Critical Care* 2005, **9(Suppl 1):**P129 (DOI 10.1186/cc3192)

**Background** Aerogen is currently developing drug/device combinations for delivery of drug to the lungs of mechanically ventilated patients with efficiencies above 60%. When therapy needs to continue post extubation, an aerosol delivery device of similar efficiency is required to deliver the same drug dose. Commercially available nebulizers with inhaled mass ranging from 6 to 30% would require several doses to achieve the same inhaled mass. We modified the pulmonary drug delivery system (PDDS; Aerogen) to provide similar drug delivery efficiencies to patients on and off the ventilator.
**Methods** Three PDDS units were used to aerosolize albuterol sulfate (2.5 mg) to simulated patients in both on vent and off vent configurations ($n = 3$). On vent was simulated with a Puritan Bennett 740 Ventilator with tidal volume of 500 ml, peak flow 40 l/min, ramp flow pattern, I:E ratio 1:2, and rate of 15 breaths/min through an 8-mm endotracheal tube attached to a passive lung model (Ingmar). The off vent configuration consisted of an adult lung simulator (Hans Rudolph) with a tidal volume of 500 ml, peak flow 28 l/min, and I:E ratio 1:2. The amount of drug deposited on an absolute filter distal to the endotracheal tube and mouthpiece was eluted and determined by reverse-phase HPLC with isocratic elution and UV detection at 275 nm. The volume median diameter (VMD) and geometric standard deviation of the aerosol were determined by laser diffraction (Spraytech™ Malvern).
**Results** The percentage of total dose ± standard deviation delivered to the test lung was 72 ± 11% on vent and 70 ± 0.3% off vent. The mean VMD was 3.5 μm with a GSD of 2.1.
**Summary** Our *in vitro* results demonstrate that it is feasible to provide comparable high-efficiency aerosol delivery to adult patients whether on or off the ventilator. Additional studies with the PDDS *in vivo* will be required to establish the *in vitro*/*in vivo* correlations of this model.
**Conclusion** The Aerogen PDDS delivered > 60% of the total dose to the airway of simulated adult patients during mechanical ventilation and spontaneous breathing.

## P130

### High-dose versus low-dose nebulized albuterol in acute asthmatic attack: a randomized double-blind clinical trial

**A Hosseinnezhad, M Abbasi**
*Rasoul Akram Medical Center, Iran University of Medical Sciences, Tehran, Iran*
*Critical Care* 2005, **9(Suppl 1):**P130 (DOI 10.1186/cc3193)

**Introduction** Asthma is a common condition, and seems to be increasing in prevalence in most countries around the world. Current guidelines for the treatment of patients with acute asthma have recommended the use of inhaled beta-agonists to reverse airflow obstruction. The optimal dose of albuterol for treatment of acute asthma has yet to be established. Most American references recommend a starting dose of 2.5 mg aerosolized albuterol every 20 min, while European authobities recommend higher doses.
**Objectives** The purpose of this study was to compare 2.5 mg with 7.5 mg nebulized albuterol for the treatment of acute asthma, using spirometric data and arterial blood gas sampling.
**Study design** A double-blind randomized clinical trial.
**Subjects** We studied 106 patients older than 15 years who presented to the emergency department with moderate to severe acute asthmatic attacks.
**Methods** On enrolment, patients underwent baseline testing, including initial spirometory/peak flowmetry and arterial blood gas sampling. A standardized treatment algorithm was used for all patients so they received oxygen and corticosteroid and underwent cardiopulmonary monitoring. Patients then received in a randomized, double-blinded fashion, nebulized albuterol at a dose of either 2.5 or 7.5 mg over 20 min. Spirometry or peak flowetry and ABG sampling were repeated after treatment. Measurements were taken of FEV1, PEFR, FVC, PH, $PCO_2$, $PO_2$.
**Results** While there was no statistically significant difference in pretreatment and post-treatment values between the two groups, there was a both clinically and statistically significant improvement in post-treatment values in each group.
**Conclusion** Overall, we may reach the conclusion that there is no advantage in the routine administration of albuterol at doses higher than 2.5 mg for adult patients with acute asthmatic attacks. It is possible that there may be an advantage in the most severely obstructed patients, although this study did not enrol enough patients with very severe asthma to evaluate this.

## P131

### Should noninvasive positive pressure ventilation be used to prevent post-extubation respiratory failure?

**P Nery, A Vasconcellos, L Pastore, G Schettino**
*Sírio Libanês Hospital, São Paulo, Brazil*
*Critical Care* 2005, **9(Suppl 1):**P131 (DOI 10.1186/cc3194)

**Rationale** The length of mechanical ventilation and the need for reintubation is associated with increased mortality. Weaning protocols are used to reduce the length of invasive ventilation. Noninvasive positive pressure ventilation (NPPV) has been suggested to shorten the length of intubation or to treat respiratory failure after extubation, but the study results are conflicting. We believe that NPPV can be useful to reduce the reintubation ratio when applied systematically and immediately after extubation in patients at risk for developing post-extubation respiratory failure.
**Objective** To evaluate the use of NPPV immediately after extubation as part of a weaning protocol.
**Methods** The data of consecutive patients mechanically ventilated for > 2 days, and who have been extubated, were collected before (pre-protocol group, 100 cases) and after the implementation of a weaning protocol (protocol group, 100 cases) in a high-complexity medical/surgical ICU. We compared the data of patients who used NPPV to treat respiratory failure in the first 48 hours after extubation (pre-protocol group) with the patients at risk for post-extubation respiratory failure (mechanical ventilation > 4 days, former T-trial failure, COPD and heart failure) who systematically used NPPV to prevent post-extubation respiratory failure (protocol group).
**Results** The population that used NPPV was similar in gender, days of mechanical ventilation before extubation (8.17 ± 6.8 vs 7.72 ± 3.78 days, $P = 0.26$) and proportion of COPD patients (28% vs 14%, $P = 0.14$) in the pre-protocol and protocol groups. NPPV was used in 70% of patients in the protocol group versus 28% of the pre-protocol ($P < 0.001$), with a lower NPPV failure ratio (reintubation < 48 hours) in proportion (10.7% vs 5.7%) but without differences in statistical analysis ($P = 0.18$). The ICU mortality for those patients who used NPPV was significantly lower in the protocol group 3.4% versus 34.8% pre-protocol ($P < 0.001$).
**Conclusion** NPPV when used immediately after extubation, as part of a weaning protocol for patients at risk for post-extubation

respiratory failure, is a safe intervention. Moreover, we report better results when comparing this technique with NPPV used to treat post-extubation respiratory failure.

### P132

### Evaluation of noninvasive mechanical ventilation with positive pressure in the management of patients with difficult weaning from invasive mechanical ventilation

**C Trevisan[1], S Vieira[1], M Blom[2], R Zancanaro[2], L Cassel[2], C Hahn[2], P Pinheiro[2]**
*[1]Clinicas Hospital, Porto Alegre, Brazil; [2]ULBRA, Canoas, Brazil*
*Critical Care* 2005, **9(Suppl 1):**P132 (DOI 10.1186/cc3195)

**Introduction** NPPV has been intensely investigated and used in patients with acute respiratory failure of several etiologies. However, recent studies have left several open questions with respect to the benefits of its use in invasive mechanical ventilation (IMV) weaning. A randomized controlled study has shown that NPPV has reduced the IMV use time in patients with persistent failure in weaning. However, some studies did not confirm these results.
**Objective** To evaluate the application of NPPV, using the Bilevel mode, in patients with IMV weaning difficulties, characterized by spontaneous ventilation failure during a spontaneous breathing trial (SBT).
**Methods** All patients under IMV for more than 48 hours from June 2003 to July 2004 were submitted to a SBT. Those that failed during the first 30 min of the T-piece trial, and without contraindications to NPPV, were randomized to be back to IMV (conventional treatment) or to be changed to NPPV. Contra-indications to NPPV included patients with facial trauma or cranial surgery, recent gastric or esophagic surgery, tracheostomy, respiratory secretion excess, agitation and noncooperative behaviour, and were excluded from the experiment. Inclusion in the experiment has been authorized by signed informed consent. Prior to subjecting the patient to the SBT we collected a sample of arterial blood gases and a measure of maximal inspiratory pressure (PImax) was taken. During spontaneous ventilation in the T-piece trial, in the first and 30th minutes measurements of tidal volume (VT), minute ventilation (Ve), respiratory rate (f), rapid shallow breathing index (f/VT), heart rate and peripheral oxygen saturation were taken. After randomizing to IMV or NPPV, patients were followed clinically and evaluated concerning time of ventilation, complications and mortality rate.
**Results** A total of 158 patients were submitted to a SBT. Among patients that failed in the T-piece trial 43 patients were eligible for this study, 21 being studied in NPPV and 22 in IMV. The mean age of the NPPV group was 68 ± 15 years, and of the IMV group was 59 ± 17 years. The average of mechanical ventilation previous to exposition to SBT was 7 days for the NPPV group and 8 days for the IMV group. The values of Ve, VT, and PImax were similar in both groups, in the first and 30th minute of ventilation in the T-piece. The average ventilation support use time, after failure in the T-piece, was 2 days for the NPPV group and 9 days for the IMV group, with statistical significance ($P < 0.05$). Total mortality was 26% (four patients in IMV and seven patients in NPPV). Considering the total number of complications, NPPV had a protective effect (RR 0.205).
**Conclusions** From these preliminary data, we believe that NPPV could be an effective treatment for patients presenting difficulties in weaning from mechanical ventilation

### P133

### Is the success of positive pressure ventilation dependent on the level of care?

**A Zito, E Meleo, F Chiappini, G Corbo, S Valente, G Ciappi**
*Università Cattolica del Sacro Cuore, Rome, Italy*
*Critical Care* 2005, **9(Suppl 1):**P133 (DOI 10.1186/cc3196)

**Objective** To report our experience with positive pressure ventilation (PPV), pressure support ventilation or assisted-controlled pressure mechanical ventilation mode, delivered by face mask (nine patients) or tracheostomy (one patient) in acute hypercapnic respiratory failure (AHRF).
**Design** An observational study.
**Setting** A respiratory care unit.
**Patients and intervention** Ten patients with AHRF, related to bronchial superinfection or pneumonia, were treated with PPV. The mean (± standard deviation) $PaCO_2$ and pH at entrance were, respectively, 95.96 ± 12.86 mmHg and 7.29 ± 0.05.
**Results** PPV resulted in a significant improvement in $PaCO_2$ (from 95.96 ± 12.86 mmHg to 73.72 ± 10.95 mmHg) and pH (from 7.29 ± 0.05 to 7.39 ± 0.05) within 2 hours. However, NIMV was discontinued in three patients (33%) after more than 5 days and endotracheal intubation was required because of inability to wean (one patient) or to manage bronchial secretions (two patients).
In the other patients NIMV was effective in improving $PaCO_2$ (from 95.96 ± 12.86 mmHg to 51.16 ± 11.75 mmHg) and pH (from 7.29 ± 0.05 to 7.40 ± 0.06). Five patients continued mechanical ventilation at home.
**Conclusion** Application of PPV is feasible outside the ICU, also when baseline pH should indicate admission to the ICU (pH < 7.25 in three patients) or the respiratory intermediate care unit (pH < 7.3 in one patient). Since all these patients but one avoided endotracheal intubation, whereas two patients with pH > 7.3 were intubated, arterial blood pH at entrance probably does not predict success or failure and it is not suitable to decide the level of care.

### P134

### Effects of the domiciliary use of benzodiazepines on the management of patients presenting to the emergency department with exacerbations of chronic obstructive pulmonary disease

**C Antro, F Merico, L Lovera, E Migliore, E Scalabrino, V Gai**
*Osp. Molinette, Torino, Italy*
*Critical Care* 2005, **9(Suppl 1):**P134 (DOI 10.1186/cc3197)

**Introduction** The use of hypnotics for sleep disturbances has been discouraged for patients with severe chronic obstructive pulmonary disease (COPD), because of potential adverse effects on ventilation. We evaluated the clinical impaction of benzodiazepine use in patients presenting to the Emergency Department (ED) with acute exacerbation of COPD.
**Methods** Of 317 consecutive patients presenting to the ED with acute dyspnoea from March to September 2004, 47 were found affected by exacerbations of COPD complicated by acute respiratory failure. Diagnosis was based on the 2004 COPD Guidelines of American Thoracic Society/European Respiratory Society. A thorough investigation (through the pharmacologic history collected from patient and/or caregivers and any available medical record) was made on each patient about the habitual use of hypnotics, particularly benzodiazepines, up until the day of admission. We evaluated mortality at discharge, need for and duration of invasive and noninvasive mechanical ventilation and

hospital length of stay in patients taking benzodiazepines (BDZ+) in comparison with those who did not (BDZ–).

**Results** Of 47 patients identified (28 males/19 females, mean age 74.7 years, APACHE II score 17.4 ± 5.3), 12 (25.5%) regularly used benzodiazepines for insomnia. Table 1 presents the APACHE II score, systolic blood pressure and arterial blood gas analysis of the BDZ– in comparison with the BDZ+.

**Table 1**

| | APACHE II score[a] | SBP (mmHg) | pH | $PaCO_2$ (mmHg) | $PaO_2$ (mmHg) | $HCO_3^-$ (mEq/l) | $PaO_2/FiO_2$ |
|---|---|---|---|---|---|---|---|
| BDZ– | 17.6 ± 4.8 | 144 | 7.32 | 63.1 | 63.1 | 30.1 | 243.4 |
| BDZ+ | 16.8 ± 6.6 | 130 | 7.33 | 64.6 | 49 | 33.5 | 216.3 |
| *P** | 0.65 | 0.03 | 0.46 | 0.8 | 0.01 | 0.1 | 0.19 |

[a]Mean ± standard deviation. * Student *t* test.

The mortality of BDZ+ was 16.6% versus 8.6% of BDZ– ($\chi^2$: $P = 0.43$); no patient was intubated, but 66% of BDZ+ underwent noninvasive ventilation versus 40% of BDZ– ($\chi^2$: $P = 0.11$). The duration of noninvasive ventilation was 23 hours 22 min for BDZ+ versus 14 hours 9 min for BDZ–: a statistically significant difference ($\chi^2$: $P = 0.04$). Hospital length of stay was 9 ± 5.5 for BDZ+ versus 15.2 ± 10.5 for the BDZ– group ($\chi^2$: $P = 0.06$).

**Conclusions** In patients with exacerbations of COPD, domiciliary use of benzodiazepines had no effect on mortality and hospital length of stay, but seemed to cause a higher need for and increased duration of noninvasive ventilation.

## P135

### Weaning from mechanical ventilation using remifentanil versus midazolam–morphine analgo sedation: our experience

**M Di Nardo, A Paperini, C Mosca, G De Durante, M Del Turco, F Giunta**

*University of Pisa, IV ICU, Department of Anesthesiology and Intensive Care, Pisa, Italy*

*Critical Care* 2005, **9(Suppl 1):**P135 (DOI 10.1186/cc3198)

**Introduction** Remifentanil is a short-acting μ-opioid with a half-life of less than 9–10 min, metabolized by plasmatic esterasis. In this retrospective study, we evaluated the safety of remifentanil sedation (RS) versus midazolam–morphine sedation (MM) in 80 patients undergoing abdominal surgery. Our target was to assess whether RS is able to reduce times of weaning from mechanical ventilation with respect to MM sedation.

**Methods** Eighty patients treated either with RS or MM were enrolled in two groups. Remifentanil infusion started at dose of 6 μg/kg/hour and titrated to reach Ramsay Sedation Scale 3–5 without the help of other drugs; supplemental midazolam bolus was administered if the patients were still agitated, instead MM was administered at the dosage of 0.01 mg/kg/hour for morphine and 0.03 mg/kg/hour for midazolam, to reach the same Ramsay Sedation Scale. The time of mechanical ventilation, weaning and adverse events (bradycardia, hypotension) were recorded in each patient during treatment and for 3 days after extubation.

**Results** Times of mechanical ventilation were the same in the two groups (94.68 ± 30.24 vs 91.04 ± 31.23, $P > 0.05$). Weaning time is significantly lower using RS than MM (31.15 ± 25.45 vs 39.51 ± 25, $P < 0.05$) Adverse effects were instead a little bit greater in the RS group than in the MM group (20% vs 12.5%).

**Conclusion** Remifentanil is well tolerated by the patients even when used for long periods in the ICU with few adverse μ-opioid effects compared with classical hypnotic-based sedation. Furthermore, remifentanil seems to decrease the time of weaning.

## P136

### Remifentanil versus sufentanil continuous infusion for sedation in mechanically ventilated patients

**G Costa, P Chiarandini, M Lugano, L Pompei, C Coccia, G Bertossi, F Ronga, N Fasano, G Della Rocca**

*Department of Anesthesia, University of Udine, Italy*

*Critical Care* 2005, **9(Suppl 1):**P136 (DOI 10.1186/cc3199)

**Introduction** The first objective of this study was to compare the effectiveness of remifentanil and sufentanil as sedative agents in mechanically ventilated patients to achieve a Ramsay sedation score (RSS) of 2–3.

**Methods** Twenty (12 males, eight females) mechanically ventilated (pressure support) patients requiring analgesia and sedation were included in the study. Patients were assigned randomly to group R (eight patients, remifentanil) or to group S (12 patients, sufentanil). In group S at ICU admission sufentanil infusion was started at 0.003 μg/kg/min. In group R at ICU admission remifentanil infusion was started at 0.05 μg/kg/min. As rescue dose a bolus of 1–2 mg midazolam was administered to reach the predefined RSS or to facilitate nursing procedures. If adequate sedation was not reached after 6 hours or before, in the case of more than three consecutive midazolam rescue dose administrations without reaching the target RSS, the continuous infusion rate was increased up to 0.01 μg/kg/min in group S and up to 0.1 μg/kg/min in group R, respectively. Neurological (RSS, GCS, VAS), hemodynamic (HR, mAP) and respiratory (TV, PEEP/Paw, RR, $PaO_2/FiO_2$, $PaCO_2$, $HCO_3^-$) data were evaluated at a predefined step from the induction of sedation (T0) and every 30 min (T30, T60, T90, T120) and then during sedation maintenance every 6 hours (T6, T12, T18, T24, T30, T36, T42, T48). After 48 hours the observation ended. Statistical analysis was performed with the Kruskal–Wallis test and comparisons with baseline values with the Dunn test. $P < 0.05$ were considered statistically significant.

**Results** RSS during the study period are reported in Figs 1 and 2. Sufentanil and remifentanil mean dosages administered were, respectively, 0.003 ± 0.001 μg/kg/min (range from 0.0009 to 0.01) and 0.07 ± 0.03 μg/kg/min (range from 0.01 to 0.18). No respiratory depression (RR < 8) was observed.

**Conclusions** These preliminary results show that either sufentanil or remifentanil are effective and safe as analgosedative agents in mechanically ventilated critically ill patients.

**Figure 1 (abstract P136)**

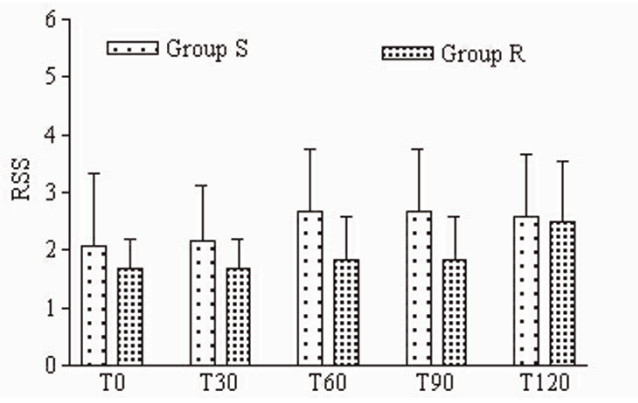
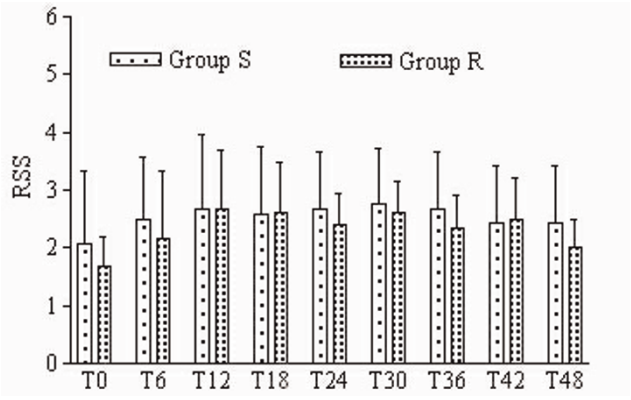


**Figure 2 (abstract P136)**




**References**
Soltész, *et al.*: *Br J Anaesth* 2001, **86:**763-768.
Jacobi J, Fraser GL, Coursin DB, *et al.*: *Crit Care Med* 2002, **30:**119-141.

## P137

### Remifentanil in neurosurgical patients in the intensive care unit

**G Koukoulitsios, C Mandila, E Paramythiotou, E Agelopoulou, G Stathopoulos, N Noulas, A Karabinis**
*General Hospital of Athens 'G Gennimatas', Athens, Greece*
*Critical Care* 2005, **9(Suppl 1):**P137 (DOI 10.1186/cc3200)

**Introduction** Remifentanil is a rapidly metabolized opioid analgesic that is being increasingly used in critically ill patients [1,2]. Our purpose was to evaluate the hemodynamic changes of sedated neurosurgery patients in the ICU caused by remifentanil as well as the time elapsed until the wakening in comparison with fentanyl and morphine. Patients received remifentanil for more than 5 days in continuous infusion.
**Methods** The study was conducted in the 12-bed ICU of a general hospital. One hundred and fifty patients of both sexes were included in the study. Their mean body weight was 77 kg. Mean duration of the surgical intervention was 180 min. After their admission to the ICU, patients were randomly assigned to three groups. Patients in group A received remifentanil 9–10 μg/kg/hour, in group B fentanyl 0.5–6 μg/kg/hour and in group C they received morphine 0.03–0.15 mg/kg/hour. Every 24 hours, sedation and analgesia were stopped for a neurological examination (Glascow Coma Scale). All patients were sedated with propofol and they remained sedated for 5 days at least. Parameters recorded were cardiac rhythm, mean arterial pressure and time to recovery (judged by spontaneous respiration).
**Results** See Table 1 for comparison of hemodynamic parameters between the three groups. Recovery time was much shorter when we compared the remifentanil group with the two other groups ($P < 0.001$). A statistically significant difference was also observed when we compared group B with group C ($P < 0.001$).
**Conclusion** We conclude that remifentanil is safe enough for neurosurgerical patients under sedation in the ICU, and that the weakening time is much shorter for patients receiving this analgesic.

**Table 1 (abstract P137)**

| | Remifentanil | Fentanyl | Morphine |
|---|---|---|---|
| Bradycardia | 3 (6%) | 2 (4%) | 2 (4%) |
| Hypotension | 8 (16%) | 6 (12%) | 2 (4%) |
| Mean arterial pressure (mmHg) | 76 | 74 | 75 |
| Mean heart rate | 68 | 70 | 71 |

**References**
1. Tipps LB, Coplin WM, Murry KR, Rhoney DH: **Safety and feasibility of continuous of remifentanil in the neurosurgical intensive care unit.** *Neurosurgery* 2000, **46:**596-602.
2. Maze M, Scarfini C, Cavaliere F: **New agents for sedation in the intensive care unit.** *Crit Care Clin* 2001, **17:**881-897.

## P138

### Risk factors, coma, and consequences of intensive care unit delirium

**Y Skrobik, M Dumont, S Ouimet**
*Hopital Maisonneuve Rosemont, Montreal, Canada*
*Critical Care* 2005, **9(Suppl 1):**P138 (DOI 10.1186/cc3201)

**Objectives** To establish risk factors for the development of delirium in an ICU, to determine the effect of ICU delirium screened with the Intensive Care Delirium Checklist on mortality and ICU and hospital lengths of stay, and to clarify the comorbidity and clinical effect of coma on the incidence of delirium and on outcome.
**Design and setting** Prospective study in a 16-bed university hospital medical/surgical ICU.
**Patients** A total of 820 consecutive patients admitted to the ICU for more than 24 hours.
**Interventions** Fifteen covariates, including medical history, severity of illness on admission (APACHE II), laboratory values, and medications were prospectively recorded for a total of 4707 patient-days (mean = 5.7 ± 7 days). All patients were screened a minimum of three times daily. Follow-up to hospital discharge was provided in all patients. Hospital length of stay, and hospital mortality, were compared between delirium and non-delirium patients. Comatose patients were arbitrarily separated into those whose coma was transient (< 5 days) or lasting (5 days or more).
**Results** Hypertensive patients, smokers, and alcoholics were more likely to develop delirium (odds ratios of 1.68, 1.56, and 1.77, respectively). Delirium was independently associated with severity of illness on admission; each additional point on the APACHE score was associated with a 4% increase in risk of delirium. Coma, regardless of its duration, increased the incidence of delirium (51% and 54% for shorter and longer duration of coma, vs 20% in patients with no coma, $P < 0.05$). The development of delirium was not associated with benzodiazepine or opiate use. Patients who developed ICU delirium were more likely to die in hospital (47% compared with 37% in patients without delirium, $P < 0.005$), and had a significantly longer length of stay (18 days compared with 13 days, $P < 0.005$). Mortality was proportional to severity of illness on admission (APACHE), presence of diabetes, total length of hospital stay and delirium occurrence.
**Conclusion** Delirium risk factors include tobacco and alcohol use, a history of hypertension, and preceding ICU coma but not ICU benzodiazepine or opiate use. Significant mortality and longer hospital stay are attributable to this morbid condition. Awareness of patients at risk may lead to better recognition and earlier intervention.
**Acknowledgement** Partial funding ($18,000) for this project was obtained from the Fonds de Recherche en Santé du Quebec.

## P139

### Evaluation of EM and orthopedic residents' pain estimation about patients with limb trauma who were visited in the Emergency Department of Hazrat Rasoul Hospital

**S Farahmand, M Ahmadi**
*Imam Khomeini Hospital, Tehran, Iran*
*Critical Care* 2005, **9(Suppl 1):**P139 (DOI 10.1186/cc3202)

**Objective** To evaluate pain estimation in the patients with limb(s) trauma by EM and orthopedic resident in the Emergency Department (ED) of Hazrat-e-Rasoul Hospital.
**Patients and methods** In a prospective study, 160 patients that merely had limb(s) trauma and were admitted to the EM ward of Hazrat Rasoul Hospital were included. Patients with GSC <15 – due to every reason, like head trauma, drug overdose, and so on – at the time of physical examination, and positive history of analgesic use before ED arrival or history of drug or alcohol abuse, were excluded from this study. At the time of the presentation to the ED, first of all the patients marked the level of their pain on a visual analogue scale (VAS) scale by supervision of the researchers and then the EM and orthopedic residents marked the pain level of every patient on a VAS, separately. The EM and orthopedic residents select randomly from on-call residents.
**Results** Of 160 enrolled cases (65 females and 95 males), the mean age was 32.05 ± 17.87 years. The mean of pain scores determined by the patients was 6.41 ± 2.52. The mean of the recorded pain scores by EM and orthopedic residents was 4.41 ± 1.83 and 4.05 ± 1.92, respectively. There was a significant difference between the mean of patients' scores and the mean of pain scores determined by both the EM and orthopedic residents, separately ($P < 0.001$); but there is no significant difference between EM and orthopedic residents. Pain estimation of EM and orthopedic residents in 20 cases were the same as the patient pain score.
**Conclusion** According to previous studies, the only accurate barometer in treating pain is the patient's report, but in our center pain treatment was done according to physicians' estimation; our study indicates that they underestimate the pain of their patients. To properly sedate patients, the VAS should be included as a routine part of vital signs and the pain score should be recorded, especially for such patients who have pain and might need painful procedures.

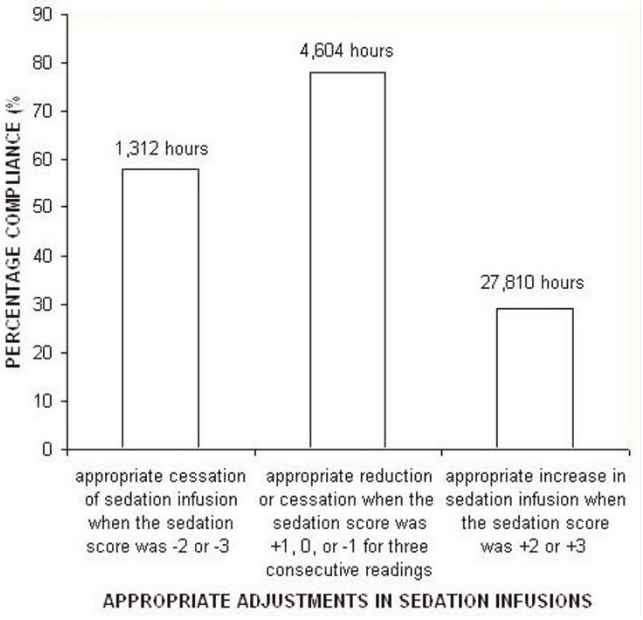
## P140

### Sedation in haemofiltered patients: a retrospective study of compliance with the sedation policy

**S Al-Saffar, R Shulman, A Webb**
*UCL Hospital NHS Foundation Trust, London, UK*
*Critical Care* 2005, **9(Suppl 1):**P140 (DOI 10.1186/cc3203)

**Aim** This study was designed to review sedation of critically ill patients requiring haemofiltration and to assess the compliance with our sedation policy.
**Introduction** Such patients are of particular concern as there is a danger of accumulation of sedatives. The UCLH sedation scale involves hourly assessment, −3 correlates with unrousable, −2 (roused by painful stimuli), −1 (roused by movement), 0 (roused by voice), 1 (aware but calm), 2 (aware and comfortable), 3 (agitated and restless). The sedation policy requires the following interventions: at +3 or +2 the dose is increased; at +1, 0 or −1 (i.e. the 'target range') no dose adjustment is attempted until three consecutive scores are achieved within the target range when dose reduction is attempted; at −2 or −3, sedation is stopped.

**Figure (abstract P140)**




Percentage of appropriate adjustments in sedation infusions.

**Method** This retrospective study was conducted in a 22-bed, mixed medical/surgical ICU in a teaching hospital. A total of 427 patients received haemofiltration between 10 September 2003 and 18 January 2004 for a total of 56,024 hours. The data for these patients who were managed with continuous sedation infusions were extracted using the UCLH Clinical Information Management System (GE Medical-healthcare QS 5.6). The level of compliance to our sedation policy was analysed by comparison with the aforementioned rules. A chi-squared test was used for statistical significance.
**Results** In 42% of oversedation hours (−2, −3) the sedative infusion was not reduced (see Fig. 1). Where sedation scores fell within the target range on three consecutive occasions sedation infusions were decreased or stopped appropriately in 78% of episodes. In undersedated hours (+2, +3), sedation infusions were increased in 29% of episodes. Sedation scores within the target range were achieved for 77.7% of the time, regardless of whether or not sedatives were given. Furthermore, sedation scores shared a similar distribution pattern in both sedated and unsedated hours except that the +1 sedation score was more prevalent in unsedated hours compared with sedated hours (1818 hours [10.9%] vs 15,451 hours [39.2%]). Episodes of undersedation were three times (3151 hours vs 1312 hours) more likely to be treated incorrectly than correctly ($P < 0.05$). In oversedated episodes, correct adjustment occurred > 3 times more often than incorrect changes (27,810 hours vs 7900 hours) ($P < 0.05$).
**Conclusion** Our data suggest that when patients were undersedated a reluctance to follow the sedation protocol by increasing the sedative dose was seen. In contrast, when patients were oversedated nurses were more inclined to follow the protocol.

## P141

### Does implementation of a goal sedation score improve management of mechanically ventilated adults?

**K Feeley[1], A Gardner[2], I Mitchell[1], A Leditschke[1]**
*[1]The Canberra Hospital, Canberra, Australia; [2]Cabrini Deakin Centre for Nursing Research, Melbourne, Australia*
*Critical Care* 2005, **9(Suppl 1):**P141 (DOI 10.1186/cc3204)

**Background** Sedation management of mechanically ventilated patients has been a source of concern for intensive care nursing and medical staff worldwide in recent years. An earlier prospective audit of 48 ventilated patients showed that our sedation management was suboptimal. Patients were oversedated 45% of the time, with the most frequent management strategy being use of morphine and midazolam infusions. Despite this, 23% of patients were physically restrained. A literature review suggested that a move away from sedative infusions would reduce the length of ventilation, length of ICU stay and tracheostomy incidence. Use of sedation scales, setting of goal sedation scores and implementation of a nurse-initiated sedation protocol were also deemed best practice.
**Objective** To determine whether introduction of a goal sedation score would be associated with improved management of sedation as indicated by a reduction in incidence of oversedation and in use of physical restraints.
**Method** The study design was prospective and exploratory. Following multidisciplinary staff training, an optimal sedation goal score was set daily by senior medical staff and changed when clinically indicated. Nurses titrated intravenous infusions of analgesia and sedation with the aim of achieving the desired goal sedation score. Sedation patterns were collected on 52 ventilated patients. Institutional ethics approval was obtained.
**Results** The median APACHE II score was 19 (range 8–33); median age was 65.9 years (range 18–88); sex ratio, male/female, was 7:3. For patients ventilated for more than 5 days only sedation patterns for the first 5 days are presented. The goal sedation score was achieved in 45% of patient-hours, with only 7% of patient-hours recorded as agitated. Incidence of oversedation was unchanged from the previous audit (45% of time). Patients deemed at risk of oversedation had a goal score compliance of 48.6%. Patients at risk of undersedation had a goal score compliance of 34.4%. When compared with prior audit results, there was an increase in the use of physical restraints from 11/48 (23%) to 21/52 (40%) (Fishers exact $P = 0.086$). Morphine and midazolam infusion use was unchanged with use in 63% and 65% of patients, respectively, and propofol was used in 73% of patients. Incidence of deliberate self-extubation was 0.9/100 ventilated days, median length of ventilation was 3.9 days and incidence of tracheostomy was 7.6%.
**Conclusion** Despite a sedation goal score being set daily, patients reached their goal score for less than one-half of ventilated hours. Oversedation continued to be a problem and may be associated with the frequent use of morphine and midazolam infusions. Considering agitation appeared to be well managed, the increased use of physical restraints is concerning. Due to the limited success of use of goal sedation scores alone to improve sedation management, we are now prospectively evaluating the use of a sedation management algorithm in conjunction with goal scores.

## P142

### The Richmond agitation–sedation scale and bispectral index during dexmedetomidine sedation

**A Turkmen, A Altan, N Turgut, S Vatansever, S Gökkaya**
*SSK Okmeydani Training Hospital, Istanbul, Turkey*
*Critical Care* 2005, **9(Suppl 1):**P142 (DOI 10.1186/cc3205)

**Introduction** Patients require continuous reassessment of their pain and need for sedation. The routine use of standardized and validated sedation scales and monitors are needed. The bispectral index (BIS) uses a monitor of cortical suppression to maintain the optimal level of sedation and hypnosis. The Richmond agitation sedation scale (RASS) has high reliability and validity in ICU patients. We aimed to assess the correlation of the BIS with the RASS during dexmedetomidine sedation.
**Methods** Eleven ventilated critically ill patients, aged 17–82 (50.09 ± 17.76) years, APACHE II score of 12.63 ± 3.90, SOFA score of 3.27 ± 1.73, were enrolled in the study. Patients received a loading dexmedetomidine infusion of 1 μg/kg over 10 min followed by a maintenance infusion of 0.5 μg/kg/hour for 8 hours. The efficacy of sedation was assessed using the RASS and BIS monitoring. The Wilcoxon test and Spearman's correlation analysis were used for statistical analysis.
**Results** Significant correlations between RASS and BIS values were found in this study (Table 1).
**Conclusion** RASS levels significantly correlated with BIS values during dexmedetomidine sedation.

**Table 1 (abstract P142)**

| | RASS 1 | RASS 2 | RASS 3 | RASS 4 | RASS 5 | RASS 6 | RASS 7 | RASS 8 |
|---|---|---|---|---|---|---|---|---|
| BIS 1 | $r = 0.77$, $P = 0.005$ | | | | | | | |
| BIS 2 | | $r = 0.87$, $P = 0.0001$ | | | | | | |
| BIS 3 | | | $r = 0.84$, $P = 0.001$ | | | | | |
| BIS 4 | | | | $r = 0.84$, $P = 0.001$ | | | | |
| BIS 5 | | | | | $r = 0.94$p, $P = 0.0001$ | | | |
| BIS 6 | | | | | | $r = 0.85$, $P = 0.001$ | | |
| BIS 7 | | | | | | | $r = 0.92$, $P = 0.0001$ | |
| BIS 8 | | | | | | | | $r = 0.90$, $P = 0.0001$ |

BIS, bispectral index; RASS, Richmond agitation sedation scale.

## P143

### The Critically Ill Adults scale

**J Schoonderbeek, P van Leeuwen, B van der Hoven, D Tibboel, M van Dijk**
*University Hospital Erasmus MC, Rotterdam, The Netherlands*
*Critical Care* 2005, **9(Suppl 1):**P143 (DOI 10.1186/cc3206)

**Introduction** An ICU stay is unfortunately associated with pain and distress. For that reason, analgesics and sedatives are prescribed in large quantities to critically ill adult patients. These patients are often not able to express their pain or distress verbally due to mechanical ventilation and sedation itself. But is treatment adequate? Because no satisfactory pain and distress instrument was found, the Critically Ill Adults (CIA) scale was developed loosely based on the COMFORT scale. Nurses were trained to use this scale. In this study the CIA was validated and cut-off scores were determined to develop useful guidelines for clinical practice.
**Method** During a 3-month period, assessments were performed in critically ill adult patients at an 18-bed general surgery/trauma intensive care unit of the University Hospital in Rotterdam, The Netherlands, a tertiary referral centre.
The newly developed CIA tool was tested and adjusted during a prior pilot study. This study resulted in deletion of physiological items and an awareness for polyneuropathy. The latter reduces body movements and therefore influences pain behaviour. The final CIA consists of five items (alertness, facial tension, muscle tone, body movements and respiratory response) with a total score of 5–20 maximally. The CIA was assessed by the researcher or care giving nurse and combined with a Numeric Rating Scale for pain intensity and distress, either filled in by the observer or the patient when self-report was feasible. The two instruments were compared and the CIA was tested before and during handling in a subsample of patients. Based on a large number of observations, cut-off scores were determined to introduce treatment guidelines.
**Results** Inter-rater reliability of 46 nurses, researchers and intensivists was excellent, with a median Cohen's Kappa of 0.86. Internal consistency of the CIA with five items was good (0.80). In 125 patients, 870 CIA and NRS scores were assessed and recorded in the Patient Data Management System. When NRS pain or distress was ≥ 4 (22.5% of all observations) the median CIA was 11 (IQR 10–13). When NRS pain or distress was below 4 the median NRS pain or distress was 9 (IQR 6–10). The median score of 9 before handling increased significantly to 11 during handling in 20 patients (Mann–Whitney U test, $P = 0.016$). A cut-off score of 10 or higher relates to good sensitivity of 0.84 and moderate specificity of 0.63.
**Conclusions** Despite beginning validity a major drawback was seen in the relatively low cut-off scores. A score of 10 could be observed when all items were scored 2, which is 'normal'. Our data suggest oversedation in these ICU patients. Further research by implementation of a CIA-based algorithm should determine whether or not this can be reduced in this specific patient population.

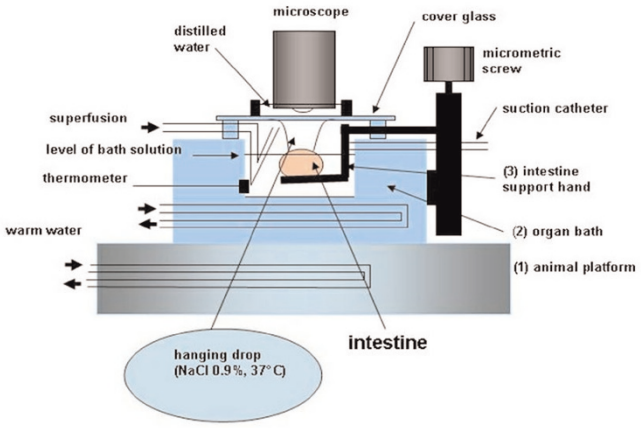
## P144

### Ketamine and propofol do not affect intestinal microcirculation in the rat edotoxemia: experiments in a new model for intravital microscopy

**M Fogliata, T Feyerherd, D Pavlovic, M Gruendling, M Wendt, C Lehmann**
*Greifswald University, Greifswald, Germany*
*Critical Care* 2005, **9(Suppl 1):**P144 (DOI 10.1186/cc3207)

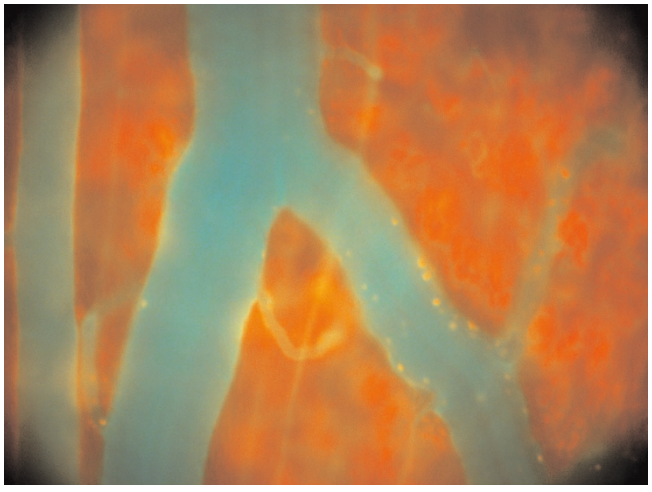
**Background** Intravital microscopy (IVM) imposes the particular problem of the combined control of the body temperature of the animal and control of the local temperature of the observed organ or tissues. We constructed and tested a new tissue support platform that employed a 'hanging drop' mechanism. Since analgesic agents are often used in sepsis and could potentially influence microcirculation, the effects of ketamine (10 mg/kg intravenously [i.v.]) and propofol (10 mg/kg bolus + 10 mg/kg/hour, i.v.) on intestinal microcirculation using fluorescent intravital microscopy in an endotoxemic rat model (lipopolysaccharide *Escherichia coli* [LPS] injection) were examined.
**Protocol** The animals ($n = 49$) were separated into six groups: control group (just microscopy), animals received LPS, only ketamine, ketamine + LPS, only propofol, and propofol + LPS. Two hours after LPS (15 mg/kg i.v.) and/or drug injection the terminal ileum was examined.

**Figure 1 (abstract P144)**




Schematic representation of the cross-section of the tissue platform disclosing the optical way.

**Figure 2 (abstract P144)**



Deep vessels (V3 venule) with sticking leucocytes (rhodamine stained) taken in the animal pretreated with endotoxine.

**Results** LPS injection did not affect the functional capillary density in the longitudinal and circular muscular and the mucosal layers but increased the number of firmly adhering leukocytes (stickers) in V3 venules (LPS vs controls; 491.2 ± 100.5 vs 187.3 ± 123.0 n/mm$^2$; mean ± standard deviation, $P < 0.05$) and in V1 venules (LPS vs controls: 256.7 ± 49.7 vs 97.9 ± 27.5 n/mm$^2$; $P < 0.05$). The number of rolling leucocytes in V3 venules was also reduced in LPS rats as compared with the control group (3.73 ± 2.7 vs 33.3 ± 28.2 n/min; $P < 0.05$). The levels of IL-1β, IL-6, IL-10 and tumour necrosis factor alpha were significantly higher in the LPS animals. The LPS induced changes were not affected by ketamine or propofol administration.
**Conclusion** The 'hanging drop' technique prevented tissue quenching, assured undisturbed microcirculation, provided stable temperature and humidity, and assured a clear visual field. It was found that LPS produced important microcirculatory changes. However, neither ketamine nor propofol affected microcirculation in endotoxemia in the rat and had no effect on the leukocyte adherence, and therefore could be used for microcirculatory studies.

## P145

### Ketamine and the coagulation response during and after cardiopulmonary bypass

**I Husedzinovic, S Barisin, N Bradic**
*Clinical Hospital Drubrava, Zagreb, Croatia*
*Critical Care* 2005, **9(Suppl 1):**P145 (DOI 10.1186/cc3208)

**Introduction** The inflammatory response and the coagulation-fibrinolytic cascades are closely interconnected. Vascular injury following cardiopulmonary bypass (CPB) may result in uncontrolled platelet activation, thrombin generation, and disseminated intravascular coagulation. Many of the anesthetic agents posses immunomodulatory effects. The clinical implications of such effects in the context of CPB remain unknown. Ketamine attenuates IL-6 response and production of the superoxide anion by neutrophils after CPB, and reduces coronary uptake of neutrophils following myocardial ishemia and reperfusion. We studied the effect of small-dose ketamine on the coagulation response (antithrombin III, fibrinogen, D-dimers, platelets) during and after CPB.
**Methods** In the preliminary prospective study report, we randomized 30 patients who underwent open heart surgery into two groups: K-group ($n = 15$), which received 0.5 mg/kg ketamine; and P-group ($n = 15$), which received placebo. Serum samples were collected before starting the operation (T0), after aorta clamp releasing (T1), 30 min (T2), 2 hours (T3), 6 hours (T4), 12 hours (T5), 24 hours (T6), and 48 hours (T7) after weaning from CPB. Data (mean ± standard deviation) were tested by variance analysis.
**Results** Both groups were comparable for age, sex, and body surface area. Differences of operative data (CPB and aorta cross-clamping time) and postoperative data (ventilatory support, ICU stay, blood transfusion) between groups were not significant. Furthermore, there was no statistical significance between all other collected data in this study.
**Conclusion** In this preliminary study, findings suggest that small doses of ketamine do not possess any effect on the coagulation response during and after CPB.

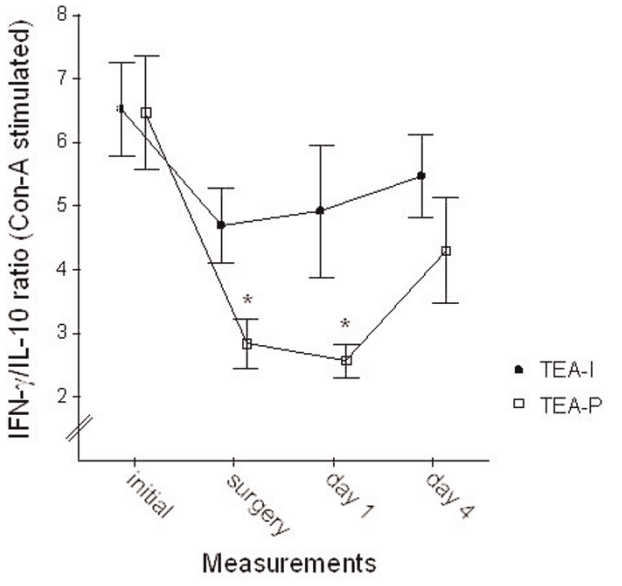
## P146

### Combined general and epidural anaesthesia improves perioperative immune function

**O Ahlers, I Kuerer, J Lenze, K Schulmeister, C Höhne, G Fritz, K Falke, D Keh**
*Charite, Campus Virchow-Klinikum, Berlin, Germany*
*Critical Care* 2005, **9(Suppl 1):**P146 (DOI 10.1186/cc3209)

**Background** Intraoperative stress may impair perioperative immune function. The hormones epinephrine, cortisol, and the stress-associated anti-inflammatory IL-10 are known to inhibit Th1 helper cells. Interferon-gamma (IFN-γ), released mainly by Th1 cells, seems to be crucial for host resistance; abolished Th1 function (anergy) is associated with increased risk of infection and mortality. We hypothesized that combined general and thoracic epidural anaesthesia (TEA) reduces intraoperative stress during major abdominal surgery preventing perioperative impairment of Th1 cells.
**Methods** Fifty-four patients undergoing major abdominal surgery were enrolled in a controlled, prospective, randomized, and single-blinded study. The protocol was approved by the local ethics committee. All patients were supported with an epidural catheter before induction of general anaesthesia. In one group ($n = 27$), the catheter was used for intraoperative analgesia (TEA-I); the other group ($n = 27$) received systemic opioids during surgery (TEA-P). Subsequently, epidural analgesia was used in both groups for postoperative pain management. Blood samples were taken before placing the epidural catheter, 2 hours after the beginning of surgery, and at days 1 and 4 after surgery. IFN-γ and IL-10 were measured in plasma and concanavalin-A (ConA)-stimulated blood samples. Stress hormone levels of epinephrine and cortisol were examined. Differences between the groups were analysed using non-parametric tests, significance was defined by $P < 0.05$.
**Results** The plasma IFN-γ/IL-10 ratio in TEA-P was lower 2 hours after the beginning of surgery (not significant). In ConA-stimulated lymphocytes, the IFN-γ/IL-10 ratio was significantly decreased in TEA-P from 2 hours after the beginning of surgery until day 1 (Fig. 1) ($P = 0.005$). This effect was mainly due to a significant

**Figure 1 (abstract P146)**



decrease of IFN-γ in TEA-P, but not due to differences in IL-10 increase. Plasma levels of epinephrine ($P = 0.022$) and cortisol ($P = 0.015$) were significantly higher in TEA-P during surgery.
**Conclusion** The intraoperative use of a thoracic epidural catheter prevents stress-induced perioperative impairment of IFN-γ release. Since IFN-γ plays a key role in host defence, the results may be of clinical relevance for the postoperative course

## P147

### Influence of thiopentone and midazolam on monocyte differentiation into dendritic cells

**C Karcher, H Raidt, H Haeberle, H Dieterich, K Unertl, T Schroeder**
*University of Tuebingen, Germany*
*Critical Care* 2005, **9(Suppl 1):**P147 (DOI 10.1186/cc3210)

**Background** Dendritic cells (DC) play a major role in the innate immune response by directing B lymphocytes and T lymphocytes. We studied the contribution of DC to the immune suppression during thiopentone and midazolam treatment. Previous *in vitro* studies have shown negative effects of thiopentone on immune function [1,2]. Clinical studies suggest that long-term sedation with thiopentone contributes to an increased incidence of nosocomial infections [3]. However, effects of thiopentone on DC have not yet been elaborated.
**Materials and methods** We investigated the effects of clinical doses of thiopentone and midazolam on the differentiation of monocytes to dendritic cells *in vitro*. Monocytes were isolated from buffy coats of healthy donors and cultured in the presence of GM-CSF and IL-4 over 8 days. The cells were incubated with different concentrations of thiopentone and midazolam, respectively. DC were characterized through surface expression of CD1a, CD14, CD16, CD40, CD80, CD83, CD86 and HLA-DR. Cell function was quantified through FITC-dextrane phagocytosis by cytometry.
**Results** In contrast to midazolam, high concentrations of thiopentone (50–100 μg/ml) led to notable alteration in the morphology and differentiation of DC. Typical morphologic characteristics like spikes and cell clustering were absent. The surface expression of CD1a was reduced by 83% (± 41%), CD40 by 93% (± 8%) and HLA-DR by 68% (± 35%). Phagocytosis capacity of these cells was decreased by 50% (± 33%).
**Conclusion** We conclude that differentiation from monocytes into DC is affected by high concentrations of thiopentone but not by midazolam. This may contribute to an immune suppression during long-term thiopentone sedation.

**References**

1. Larsen B, Hoff G, Wilhelm W, *et al.*: *Anesthesiology* 1998, **89:**1218-1227.
2. Heller A, Heller S, Blecken S, *et al.*: *Acta Anaesthesiol Scand* 1998, **42:**518-526.
3. Bronchard R, Albaladejo P, Brezac G, *et al.*: *Anesthesiology* 2004, **100:**234-239.

## P148

### Propofol and methohexital comparably affect polymorphonuclear leukocyte function in patients after cardiac surgery

**E Hüttemann, M Büttner, K Vogelsang, S Sakka**
*Friedrich-Schiller-University Jena, Germany*
*Critical Care* 2005, **9(Suppl 1):**P148 (DOI 10.1186/cc3211)

**Background** Experimental and clinical studies suggest that anesthetics have a variety of negative side effects on polymorphonuclear (PMN) leukocytes, which play a vital role in the defense against invading bacteria. In this study, we analyzed the effects of propofol and methohexital on PMN leukocyte function in patients after cardiac surgery.
**Patients and methods** In this observational clinical study, we studied 46 patients undergoing elective cardiac surgery who postoperatively either received propofol ($n = 29$) or methohexital ($n = 17$). Patients in the propofol group (P) (19 males, 10 females) had a mean age of 65 ± 11 (range 36–80) years. In the methohexital group (M) (12 males, five females) the mean age was 65 ± 8 (range 43–77) years. Both sedatives were administered according to clinical requirements. PMN leukocyte function was assessed as respiratory oxidative burst and expressed as the percent of oxidating cells (normal 70–100%). Furthermore, the mean fluorescence intensity (MFI) was determined as a measure of intracellular uptake of bacteria. Both variables were assessed before induction of anesthesia (MP1), on ICU admission after cardiac surgery (beginning of sedative administration) (MP2), 6 hours after ICU admission (MP3) and 24 hours after beginning of anesthesia (MP4). Patients' demographics and measurement results were compared by *t* test and analysis of variance for repeated measures.
**Results** Both groups were well matched in terms of patient demographics, age, body weight and duration of sedative administration (P: 9.4 ± 5.4 hours vs M: 8.4 ± 5.6 hours). Within both groups, respiratory oxidative burst significantly decreased over time (MP1 and MP2 vs MP3 and MP4, respectively). For comparison, respiratory oxidative burst at MP4 was significantly higher for methohexital (82%) than propofol (72%). While oxidation decreased between MP3 and MP4 for propofol, no significant change was observed between these two time points for methohexital. For MFI, a time-dependent decrease was found for both drugs, without any difference between both groups.
**Conclusions** PMN leukocyte function is comparably depressed by propofol rather than methohexital in patients after cardiac surgery.

## P149

### Effects of propofol versus methohexital on neutrophil function and immune status in critically ill patients

**S Sakka, A Jung, H Vogelsang, E Huettemann**
*Friedrich-Schiller-University Jena, Germany*
*Critical Care* 2005, **9(Suppl 1):**P149 (DOI 10.1186/cc3212)

**Introduction** Sedatives (i.e. propofol and methohexital) have a variety of negative side effects on neutrophil leukocytes, lymphocytes and monocytes, which all play a vital role in the defense against invading microorganisms [1]. In this study, we investigated these effects in critically ill patients with long-term sedation.
**Patients and methods** In this observative clinical study, we analyzed 21 critically ill patients with long-term sedation who either received propofol ($n = 12$, APACHE II score 26 ± 4) or methohexital ($n = 9$, APACHE II score 28 ± 6) after ICU admission. Patients in the propofol group (P) (nine males, three females) had a mean age of 55 ± 15 years. In the methohexital group (M) (eight males, one female) the mean age was 48 ± 18 years. Both sedatives were administered according to clinical requirements. Neutrophil leukocyte function was assessed as phagocytosis and respiratory oxidative burst activity. Furthermore, cellular markers of monocytes and lymphocytes (CD3, CD4, CD8, CD19, CD57, CD122) were assessed. Measurements were made on ICU admission, day 3, day 7 and day 14 of drug administration. Patients' demographics and results were compared by Mann–Whitney U test and one-way repeated-measures analysis of variance with an all pair-wise multiple comparison procedure.

**Results** Both groups were well matched in terms of age, height and body weight. ICU length of stay was comparable (22 ± 7 days vs 20 ± 9 days). Mortality was 0/12 and 2/9, respectively. Absolute numbers of leukocytes and subpopulations were comparable between both groups at each time point. We found no difference in neutrophil oxidative burst and phagocytosis within and between both groups at the different time points. With respect to lymphocyte and monocyte CD marker expression, no differences within each group and between the time points were found.

**Conclusion** Effects of methohexital and propofol on neutrophil leukocyte function, expression of lymphocyte and monocyte markers were not different in critically ill patients with long-term sedation.

**Reference**

1. Kelbel I, Weiss M: **Anaesthetics and immune function.** *Curr Opin Anaesthesiol* 2001, **14:**685-691.

## P150

## HLA-DR expression on monocytes and the T-cell subset in septic patients

**N Menestrina, A Martini, A Milan, G Soldati, C Parolini, G Finco, L Gottin**

*Ops Poloclinico GB Rossi, Verona, Italy*

*Critical Care* 2005, **9(Suppl 1):**P150 (DOI 10.1186/cc3213)

**Introduction** Sepsis is one major cause of mortality in the ICU, despite increasing knowledge about its physiopathology, new generation of antibiotics and an advance in supportive therapy [1]. Interaction between microorganisms and toxins produced an activation of the immune system, resulting in release of proinflammatory and anti-inflammatory cytokines. Recent studies demonstrated an imbalance in the immune system during sepsis due to a high level of antinflmmatory cytokines, with a decrease of major histocompatibility leukocyte antigen (HLA-DR) on monocytes and alteration on total lymphocyte phenotype frequency.

**Aim** To determine the time of HLA-DR expression in peripheral blood monocytes, variation in the lymphocyte subset, and their relationship with markers of inflammation, gravity score and development of sepsis.

**Design** A prospective, longitudinal study.

**Setting** A university hospital ICU.

**Patients** Twenty consecutive medical patients admitted to the ICU, 13 with sepsis and seven noninfected, without haemopoietc cancer, immunodepression and chronic therapy with steroids.

**Interventions** Daily SOFA score, IPS score and clinical sepsis criteria as defined by the ACCP/SCCM were checked. Serum procalcitonin, C-reactive protein, leukocyte antigens and lymphocyte subset features were serially recorded every day after arrival during all periods of stay in the ICU.

**Measurements and results** The percentage of HLA-DR on monocytes was significantly depressed in septic patients, particularly related to worsening of disease. In patients with septic shock the lowest value of HLA-DR on monocytes was recorded; that value increases with resolution of sepsis-correlated organ failure. The area under the ROC curve for HLA-DR to discriminate sepsis was 0.86 (sensibility 94% and specificity 61% with cutoff 0.7). The CD4/CD8 T-cell ratio was reduced in septic patients compared with nonseptic patients; the nadir value was in patients with septic shock as the HLA-DR value. Procalcitonin, C-reactive protein and gravity scores were correlated with monocytic HLA-DR expression and CD4/CD8 T-cell ratio.

**Conclusion** A decrease of monocyte expression of HLA-DR and the CD4/CD8 T-cell ratio occurred during infection disease. In septic shock signs of uncontrolled hyperinflammation are contemporary with a severely depressed cellular response. HLA-DR has a good sensibility and specificity to differentiate sepsis from other noninfectious conditions in critically ill patients.

**Reference**

1. Dellinger RP, Carlet JM, Masur H, *et al*.: **Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock.** *Crit Care Med* 2004, **32:**858-873.

## P151

## Serum cholesterol level: is it a marker of sepsis?

**B Abraham, J Raja, N Ramakrishnan**

*Department of Critical Care Medicine, Apollo Hospitals, Chennai, India*

*Critical Care* 2005, **9(Suppl 1):**P151 (DOI 10.1186/cc3214)

**Background** There is no ideal biomarker for sepsis. Recent studies have linked cholesterol levels with critical illness [1]. This study has been conducted to document the baseline cholesterol level in critically ill patents and to correlate its trend with the development, progression and outcome of sepsis.

**Method** Prospective analysis of laboratory and clinical data of 184 consecutive patients admitted to a 64-bed critical care unit (CCU) of a tertiary care hospital in South India. Data collected were the demographics, and the cholesterol level at the time of admission, at the onset of sepsis (with or without multiorgan failure) and on discharge from the unit. Sepsis was defined as per the 1992 ACCP consensus conference criteria. MOD scoring was done daily. Patients who were admitted with sepsis and those who developed sepsis during their stay in the unit were considered as the study group, while those who did not develop sepsis acted as the control group. Data were expressed as mean ± standard deviation. The paired Student's *t* test was used to compare the total cholesterol levels between the two groups. Correlation coefficient and logistic multiple regression analysis was performed with the MOD score, cholesterol levels and mortality. $P < 0.05$ was considered significant.

**Results** A total of 183 patients were enrolled into the study (study group – 73 and control – 110). The mean age was 56.4 ± 18.7 years and the male/female ratio was 1.8:1. The mean admission cholesterol was 212.5 ± 56 mg/dl, while the mean cholesterol level on day 5 was 112.3 ± 34.5 mg/dl in the sepsis group and 179.4 ± 47.6 mg/dl in the control group. The lowest cholesterol levels recorded were in patients who died in the study group: 101.3 ± 18.1 ($n = 54$). The cholesterol level at the time of discharge from the CCU in the study group ($n = 19$) was 109.74 ± 20.7 and in the control group ($n = 102$) was 201 ± 51.3

**Discussion** The drop in cholesterol levels during the CCU course shows a correlation with the onset of a new infection and development of sepsis. Lower cholesterol levels were associated with increasing mortality. Convalescence/discharge from CCU was associated with improvement in cholesterol levels.

**Conclusion** This study reveals the negative prognostic value of hypocholesterolemia in critical illness. It is a sensitive marker for onset of infection and sepsis.

**Reference**

1. van Leeuwen HJ, Heezius EC, Dallinga GM, van Strijp JA, Verhoef J, van Kessel KP: **Lipoprotein metabolism in patients with severe sepsis.** *Crit Care Med* 2003, **31:**1359-1366.

## P152

### Serum lipoproteins: how important are they in septic shock patients? Is there a relation to outcome?

**M Theodorakopoulou[1], N Skabas[2], M Lignos[1], M Theotokas[2], S Ioannidou[2], M Nikandros[2], A Armaganidis[1]**
*[1]Attiko University Hospital, Athens, Greece; [2]3rd Hospital of Ika, Athens, Greece*
*Critical Care* 2005, **9(Suppl 1):**P152 (DOI 10.1186/cc3215)

**Introduction** Decreased concentrations of serum lipoproteins occur early in critically ill patients. Furthermore, very little is known of the role that lipoproteins play in septic shock. Lipoproteins have recently been associated with innate immunity. It is reported that low values of lipoproteins are associated with low innate immunity and poor prognosis. A prospective study was designed to evaluate serum lipoproteins in septic shock patients and to investigate possible relations to the outcome.
**Methods** A prospective study over a period of 1 year set in a six-bed university hospital intensive care unit and in a five-bed medical intensive care unit of a tertiary care hospital. Eighty-eight patients were included in the study that met the ACCP/SCCM consensus criteria for septic shock. Blood samples were collected from these patients on days 1, 3, 6, 9, 12 and 15 or until discharge or death and were analyzed for total cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL) and triglycerides. Results are expressed as mean ± standard deviation. Multiple level regression analysis was used.
**Results** The group of patients were divided into survivors and nonsurvivors. We had 33 patients in the nonsurvivor group and 55 patients that recovered from their septic shock. The mortality rate was approximately 37.5%. The APACHE II scores for both groups were similar with no significant difference during the study. Admission values of serum lipoproteins showed no significant differences in either group of patients. However, a statistically significant difference was observed between the groups from day 3. Serum cholesterol, HDL levels were significantly lower starting from day 3 and triglyceride levels were significantly higher noted also from day 3 and onwards. All serum lipoproteins showed statistically significant differences between the two groups from day 6 and onwards. LDL showed no significant difference between the two groups.
**Conclusion** In our study it was evident that low cholesterol and low HDL levels as well as high triglyceride levels are significantly related to poorer outcome in septic patients. All three variables presented a significant difference between survivors and non-survivors during the study.

## P153

### Association of prior statin therapy with cytokine profiles and outcomes in patients hospitalized with community acquired pneumonia

**E Milbrandt, J Kellum, L Kong, L Weissfeld, J Martinez, D Angus, for the GenIMS Investigators**
*The CRISMA Laboratory, Department of CCM, University of Pittsburgh, Pittsburgh, PA, USA*
*Critical Care* 2005, **9(Suppl 1):**P153 (DOI 10.1186/cc3216)

**Introduction** Two small studies found prior statin use was associated with decreased ICU admission and severe sepsis in patients hospitalized with bacterial infection and decreased mortality in bacteremic patients. These effects were postulated to be due to anti-inflammatory effects of statins. We examined prior statin use, plasma cytokine levels, and outcomes in a large cohort of patients hospitalized with community acquired pneumonia (CAP).
**Hypothesis** We hypothesized that prior statin use would be associated with: ICU admission, severe sepsis, and hospital mortality; and altered plasma cytokine levels.
**Methods** This study was part of Genetic and Inflammatory Markers of Sepsis (GenIMS), a prospective observational cohort study of patients presenting to the Emergency Department with CAP in 28 US hospitals. Demographics, illness severity, and statin use within 7 days of presentation were determined at baseline and patients were followed to determine rates of hospital and ICU admission, severe sepsis, and hospital mortality. Plasma cytokine levels (tumor necrosis factor, IL-6, IL-10) were obtained daily in hospitalized patients. Outcomes were compared for prior statin (S) versus no statin (No S) use in all hospitalized CAP patients and in those who developed severe sepsis. Cytokine levels were assessed using a mixed-model longitudinal analysis.
**Results** Of the 2320 patients enrolled, there were 1895 hospitalized with confirmed CAP. Of those, there were 426 (22.5%) S and 1469 (77.5%) No S patients. S patients were older (72.2 vs 66.5 years, $P < 0.001$) and sicker, with higher comorbidity (2.2 vs 1.9, $P = 0.003$) and APACHE III (58.2 vs 55.7, $P = 0.01$) scores. S patients had increased rates of severe sepsis (51.9% vs 45.7%, $P = 0.03$), but similar ICU admission (18.3% vs 15.2%, $P = 0.13$) and hospital mortality (3.3% vs 5.0%, $P = 0.14$). After adjustment for age, gender, PSI, comorbidity, chronic organ dysfunction, SOFA, and APACHE III scores, S patients had greater odds of ICU admission (odds ratio [OR] 1.44, $P = 0.02$), but not severe sepsis (OR 1.19, $P = 0.20$) or mortality (OR 0.71, $P = 0.28$). Among those with severe sepsis, there were 221 (24.7%) S and 672 (75.3%) No S patients, with no baseline difference between groups except for slightly less chronic organ dysfunction in S patients ($P = 0.01$). S patients trended toward lower mortality (6.3% vs 10.7%, $P = 0.056$) in univariate analysis, but not after adjusting for baseline covariates (OR 0.68, $P = 0.23$). Among those with severe sepsis, IL-10 ($P = 0.03$) and tumor necrosis factor ($P = 0.03$), but not IL-6 ($P = 0.91$) were significantly lower in S patients. There were no cytokine differences in the larger hospitalized CAP cohort.
**Conclusions** In a large cohort of hospitalized CAP patients, both proinflammatory and anti-inflammatory cytokine levels were lower in S patients with severe sepsis, but we were unable to confirm the protective effect of prior statin use for clinical outcomes seen in smaller studies.

## P154

### Compartmentalized anti-inflammatory effects after topical activation of fibinolysis by tissue plasminogen activator in experimental polymicrobial peritonitis

**S van Veen, A van Vliet, T van Gulik, M Boermeester**
*Academic Medical Center, University of Amsterdam, The Netherlands*
*Critical Care* 2005, **9(Suppl 1):**P154 (DOI 10.1186/cc3217)

**Introduction** During secondary peritonitis, intra-abdominally formed fibrin entraps bacteria that are thereby difficult to eliminate by host defence mechanisms. Activating fibrinolysis may have beneficial effects on bacterial clearance and thus on inflammatory responses. Systemic fibrinolysis has risks of major bleeding complications. In this study, tissue-type plasminogen activator (tPA) was administered topically 24 hours after induction of peritonitis to examine the effects of fibrinolysis on local (abdominal) and distant (circulatory and pulmonary) inflammatory responses during polymicrobial peritonitis.
**Methods** C57BL/6 mice underwent cecal ligation and puncture (CLP) or sham operation with, after 24 hours, relaparotomy and

therapeutic peritoneal lavage with either saline or tPA (0.5 mg/ml). Inflammatory response, coagulation and fibrinolysis were assessed in peritoneal fluid, systemic circulation and lung compartments.
**Results** CLP increased bacterial load, neutrophil influx and activity, coagulation and fibrinolysis compared with sham (all parameters $P < 0.01$). Compared with saline lavage, tPA lavage reduced intra-abdominal bacterial load, KC concentration and thrombin–anti-thrombin complexes (all $P < 0.05$), and also reduced intra-abdominal as well as pulmonary neutrophil influx and activity, and clotting times (all $P < 0.05$). Mediator levels of fibrinolysis were not significantly altered by tPA; histology showed less fibrin depositions concomitant with reduced peritoneal, liver and lung damage after tPA lavage ($P < 0.05$). Mortality decreased from 50% to 35% ($P = 0.3$). Different kinetics were seen when comparing abdominal and pulmonary compartments.
**Conclusions** In this model of polymicrobial peritonitis, abdominal activation of fibrinolysis by tPA lavage effectively reduced intra-abdominal bacterial load, thereby reducing inflammatory responses in abdominal and extra-abdominal compartments and remote fibrin deposits and tissue damage. Different kinetics between peritoneal, systemic and pulmonary compartments suggested compartmentalised responses.

## P155

### Endotoxin enhances the fibrinolytic activity of monocytes incorporated in a fibrin clot

**A Grosjean[1], K Zouaoui Boudjeltia[1], M Piagnerelli[2], M Vanhaeverbeek[1]**
*[1]ULB, Montigny-le-Tilleul, Belgium; [2]ULB – Erasme Hospital, Brussels, Belgium*
*Critical Care* 2005, **9(Suppl 1):**P155 (DOI 10.1186/cc3218)

**Background** In sepsis, one of the most important problems is the modification of the hemostasis balance with activation of the coagulation. This is due, in part, to increased expression of tissue factor at the monocyte surface [1]. In these patients, we also observe a systemic hypofibrinolysis [2]. However, it is known that leukocytes have a profibrinolytic potential [3].
**Aim** To explore the role of monocytes in the fibrinolytic balance.
**Materials and methods** THP-1, a monocytoïd cell line, was challenged or not with 10 µg/ml lipopolysaccharide during 4 hours, before being introduced in an euglobulin clot lysis time assay, measured by a new semi-automatic method [4]. Resting cells were introduced in the assay at concentrations ranging from $0.25 \times 10^6$ cells/ml to $10^6$ cells/ml and stimulated cells at the concentration of $10^6$ cells/ml. Control without cells is the baseline. Statistics used analysis of variance.
**Results** First, we observed a gradual diminution of lysis time with resting cells, from 12% to 25% of the baseline, according to the concentration of cells ($n = 6$; $P < 0.001$). Then, when we added stimulated THP-1, we observed a greater diminution of lysis time: 31% of the baseline ($n = 8$; $P < 0.001$ from the baseline and $P < 0.05$ from resting cells).
**Conclusion** Monocytes play a role in the fibrinolytic balance and this role is enhanced when they are activated by lipopolysaccharide, like in sepsis. In the future, we will have to investigate why monoyctes are responsible for such an antagonism, stimulating coagulation and fibrinolytic processes, at the same time.
**References**
1. Gregory SA, Morrissey JH, Edgington TS: **Regulation of tissue factor gene expression in the monocyte procoagulant response to endotoxin.** *Mol. Cell Biol* 1989, **9:**2752-2755.
2. van Deventer SJH, Büller HR, Ten Cate JW, Aarden LA, Hack CE, Sturk A: **Experimental endotoxemia in humans: analysis of cytokine release and coagulation, fibrinolytic and complement pathways.** *Blood* 1990, **76:**2520-2526.
3. Rulot H: **Intervention des leucocytes dans l'autolyse de la fibrine.** *Arch Int Physiol* 1904, **1:**152-158.
4. Zouaoui Boudjeltia K, Cauchie P, Remacle C, Guillaume M, Brohee D, Hubert JL, Vanhaeverbeek M: **A new device for measurement of fibrin clot lysis: application to the euglobulin clot lysis time.** *BMC Biotechnol* 2002, **2:**8.

## P156

### Is fibrinolysis a predictive marker of multiple organ failure in critically ill patients?

**Y Bouckaert[1], K Zouaoui Boudjeltia[2], M Piagnerelli[1], J Ducobu[3], M Vanhaeverbeek[2]**
*[1]Hôpital Erasme, Bruxelles, Belgium; [2]A Vésale Hospital, Montigny-le-Tilleul, Belgium; [3]CHU Tivoli, La Louvière, Belgium*
*Critical Care* 2005, **9(Suppl 1):**P156 (DOI 10.1186/cc3219)

**Background** C-reactive protein (CRP) is correlated with the risk of multiple organ failure (MOF) and death in intensive care patients [1]. CRP inhibits fibrinolysis by inducing plasminogen activator type 1 release by endothelial cells [2]. We observed a link between CRP and fibrinolysis at ICU admission [3].
**Objective** We aimed to evaluate the relationship between CRP and fibrinolysis and the potential predictive value of fibrinolysis at admission in the ICU on the development of MOF.
**Methods** Thirty-eight patients were enrolled. The plasma fibrinolytic capacity was assessed by the euglobulin clot lysis time (ECLT) determined by a semi-automatic method [4]. The ECLT, CRP and the SOFA score were measured on admission (time 1) and between the third and the fifth day (time 2) of the ICU stay.
**Results** The ECLT was higher in septic than nonseptic patients ($970 \pm 928$ min versus $503 \pm 304$ min [$P = 0.042$]). Platelet count remained stable between the two times. We found a correlation between ECLT on admission and SOFA score at time 2 ($r = 0.67$; $P < 0.001$). There was no link between ECLT and the mortality rate ($P = 0.68$). CRP was correlated with ECLT during the ICU stay (time 1: $r = 0.74$, $P < 0.001$; time 2: $r = 0.60$, $P < 0.001$).
**Conclusion** The ECLT at admission could be a good predictive marker for the development of MOF between the third and the fifth day of the ICU stay.
A correlation exists between CRP and the ECLT during all the ICU stay. This finding is compatible with a link between inflammation and fibrinolysis and may explain the negative prognostic value of high concentrations of CRP in critically ill patients.
**References**
1. Lobo SMA, *et al.*: *Chest* 2003, **123:**2043-2049.
2. Devaraj S, *et al.*: *Circulation* 2003, **107:**398-404.
3. Zouaoui Boudjeltia K, *et al.*: *Thromb J* 2004, **2:**7.
4. Zouaoui Boudjeltia K, *et al.*: *BMC Biotechnol* 2002, **2:**8.

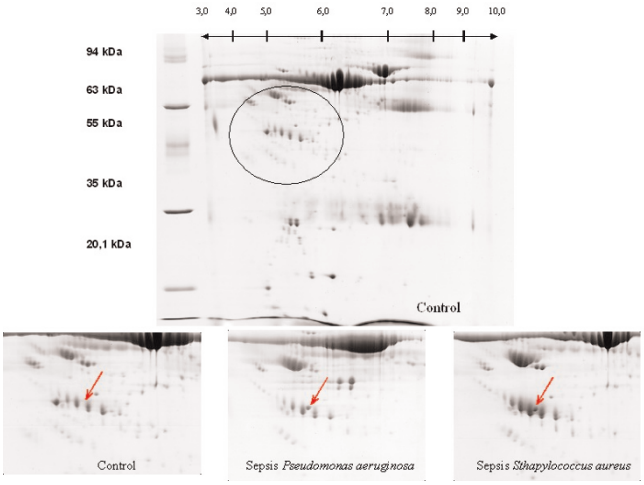
## P157

### A proteomic study of sepsis

**A Soares, M Santos, M Junqueira, C David, G Domont**
*HFAG, Rio de Janeiro, Brazil*
*Critical Care* 2005, **9(Suppl 1):**P157 (DOI 10.1186/cc3220)

**Introduction** Sepsis, characterized by intense reaction of the organism, due to infection, particularly of the inflammatory and coagulation systems, is a common illness, of high cost treatment and deaths. Thus, new technologies for the detection of sepsis early-stages are urgently needed. Our objective was to identify serum proteomic patterns that would distinguish sepsis patients from healthy controls.
**Materials and methods** Six ICU patients that matched the criteria (ACCP/SCCM) for sepsis diagnosis were selected: male/female,

**Figure 1 (abstract P157)**




3/3; mean/range age of 81.1/68–89 years; mean LOS_ICU of 15 ± 25 days; 28-day mortality (dead/total/%) = 4/6/66%; mean APACHE II score of 22 (20–26); and mean SOFA = 6 (5–8); VAP (*Pseudomonas aeruginosa*, three patients) and CRBSI *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Candida albicans* (one each). Serum samples were submitted to isoelectric focusing of proteins in the first dimension with a nonlinear strip of pH 3–10 and in the second to 12.5% 2D-SDS-PAGE. Gels were stained with Coomassie Blue and the final image analyzed using the Image Master Platinum software (Amersham). Selected spots were cut, washed, dried, swollen with trypsin solution and incubated for 16 hours at 37°C. The peptides were extracted, concentrated and analyzed by mass spectrometry in a MALDI-TOF Voyageur DE-PRO instrument (ABI). Peptide maps were processed (MS-Fit, Protein Prospector) for protein identification in the NCBI Data Bank.

**Results** Image analyses of the gels showed the presence of spots only in patients with sepsis (Fig. 1, arrows) and the presence of other spots with different intensities in sepsis and controls. Peptide mass fingerprinting of some of these spots identified actin, zinc-finger protein, matrin 3, haptoglobin-2 and apolipoprotein A1.

**Discussion** Actin, a major component of the cytoskeleton, is found in cellular injury as in apoptosis; zinc-finger protein is expressed in cellular injury as a cytoprotective protein with anti-apoptosis activity; matrin 3 functions in transcription and interacts with other proteins of the cellular matrix; apolipoprotein A1 is capable of directly inactivating endotoxin (protein–endotoxin interaction); haptoglobin-2 is present during the acute phase reaction. These findings justify the use of proteomic techniques as a screening tool for the study of all stages of sepsis in high-risk patients.

## P158

### Circulating levels of the long pentraxin PTX3, an acute phase mediator of innate immunity, in acute lung injury/acute respiratory distress syndrome: functional and prognostic correlations

**T Mauri[1], M Bombino[1], E Bertoli[1], A Doni[2], A Mantovani[2], A Pesenti[1]**
*[1]University of Milan-Bicocca, Hospital St Gerardo, Monza, Giussano, Italy; [2]University of Milan, Istituto Mario Negri, Milan, Italy*
*Critical Care* 2005, **9(Suppl 1):**P158 (DOI 10.1186/cc3221)

Acute lung injury/acute respiratory distress syndrome (ALI/ARDS) is characterized by an important inflammatory reaction involving both lungs, often spreading systemically. Pentraxin 3 (PTX3) has recently been described as a mediator of the acute phase of innate immunity. It belongs, together with C-reactive protein (CRP), to the pentraxin superfamily. PTX3 is produced by endothelial cells, fibroblasts, mononuclear phagocytes and dendritic cells in response to primary inflammatory signals (IL-1, tumor necrosis factor, LPS). Its involvement in the pathogenesis of ALI/ARDS seems probable and potentially interesting for the pathophysiology, the diagnosis and possibly the therapy of the syndrome.

We measured PTX3 levels, by an ELISA test, in the sera of 25 patients affected by ALI/ARDS. We also collected data related to etiology, pulmonary mechanics, gas exchange, systemic inflammatory involvement, microbiology, blood cells and the outcome of these patients.

PTX3 was markedly elevated in all 25 patients (average 111.07 ± 192.01 ng/ml; range 4.94–922.91 ng/ml). In no patient were PTX3 levels lower or equal to the physiological threshold of 2 ng/ml.

Levels of logPTX3 were significantly different between survivor and nonsurvivor patients (1.465 ± 0.529 log ng/ml vs 1.950 ± 0.643 log ng/ml; $P = 0.05$).

Patients with two or more organ failures (besides the lung) also had logPTX3 levels significantly higher than patients with just one additional organ failure (1.936 ± 0.597 log ng/ml vs 1.423 ± 0.542 log ng/ml; $P < 0.04$). The same was true when PTX3 levels in patients with septic shock were compared with PTX3 levels in patients without shock (262.465 ± 350.727 ng/ml vs 63.257 ± 70.261 ng/ml; $P < 0.03$).

PTX3 and logPTX3 were correlated with body temperature ($r = 0.56$ $P < 0.01$; $r = 0.51$ $P = 0.01$) and with arterial blood pH ($r = -0.53$ $P < 0.01$; $r = -0.53$ $P < 0.01$).

We have underlined a relationship between circulating levels of PTX3 and some markers of the severity of systemic involvement. PTX3 could be an indicator of the gravity of the systemic inflammatory reaction and of unfavourable outcome in ALI/ARDS patients.

## P159

### Soluble haemoglobin scavenger receptor (sCD163): a marker associated with bacteraemia

**S Gaïni[1], S Pedersen[1], S Moestrup[2], C Pedersen[1], H Møller[3]**
*[1]Odense University Hospital, Odense, Denmark; [2]University of Aarhus, Denmark; [3]Aarhus University Hospital, Aarhus, Denmark*
*Critical Care* 2005, **9(Suppl 1):**P159 (DOI 10.1186/cc3222)

**Objective** Soluble haemoglobin scavenger receptor (sCD163) is a macrophage-specific marker, and elevated levels have been observed in patients with pneumonia and sepsis. The objective of our study was to evaluate sCD163 as a diagnostic and prognostic marker in patients with community acquired sepsis.

**Design** A prospective observational study.

**Methods** One hundred and ninety-four adult patients admitted to a Department of Internal Medicine at a tertiary hospital with suspected community acquired infections. Daily blood sampling for sCD163 analysis was performed for up to 5 days. Laboratory analyses were performed with a sandwich ELISA using polyclonal rabbit anti-CD163 as the catching antibody and monoclonal anti-CD163 as the secondary antibody. The patients were classified according to SIRS criteria. The patients were divided in the following groups: patients with no proven infection ($n = 67$, control group), patients with possible infection ($n = 21$, not included in analysis), patients with proven infection without SIRS ($n = 25$), patients with sepsis ($n = 52$), patients with severe sepsis ($n = 29$). Only one patient had septic shock. Twelve patients had

bacteraemia. Demographic data, comorbidity, microbiological aetiology, biochemical parameters, focus of infection, severity score and mortality on day 28 were recorded.

**Results** The median age was 68 years (range 18–92). The male–female ratio was 0.84. The mortality rate among infected patients on day 28 was 3.8%. sCD163 concentrations are presented as medians and range: 2.9 mg/l (1.22–12.65) in patients with no proven infection, 3.75 mg/l (1.59–74.04) ($P = 0.04$) in patients with infection without SIRS, 3.02 mg/l (0.54–22.51) (not significant) in patients with sepsis, 4.05 mg/l (1.71–28.4) ($P < 0.01$) in patients with severe sepsis, 4.92 mg/l (2.66–28.4) ($P < 0.01$) in patients with bacteraemia.

**Conclusions** Elevated levels of sCD163 were observed in patients with infection without SIRS, in patients with severe sepsis and in patients with bacteraemia. The sepsis group had sCD163 levels comparable with the noninfected control group. The highest levels of sCD163 were associated with the presence of bacteraemia. Further studies are needed to unravel the role of sCD163 in severe infections.

## P160

### Measurement of granulocyte colony-stimulating factor and IL-6, IL-8 and IL-10 as an early predictor for septic patients

**A Abdel Razek, N Kobbia, E Abdel Moneim, G Abdel Nabi**
*Alexandria Faculty of Medicine, Alexandria, Egypt*
*Critical Care* 2005, **9(Suppl 1):**P160 (DOI 10.1186/cc3223)

**Introdcution** Despite the great evolution in the treatment modalities of sepsis, there is an unsatisfactory improvement in the mortality rate. Cytokines play an important role in occurrence of SIRS, sepsis and multiple organ failure. A series of proinflammatory cytokines such as IL-1, IL-6, and IL-8 are secreted early in sepsis followed by another group of anti-inflammatory cytokines such as IL-10 and granulocyte colony-stimulating factor (G-CSF).

**Objective** This study was carried out to find the benefit of early measurement of serum IL-6, IL-8, IL-10 and G-CSF for diagnosis of sepsis and its impact on patient outcomes in septic patients.

**Patients and methods** Eighty patients (50 males and 30 females) fulfilling the criteria of SIRS were categorized on admission according to ACCP&SCCM definition into four groups: SIRS (26 patients), septic patients (26 patients), severe sepsis (14 patients), and septic shock (14 patients). Their age ranged between 19 and 75 with a mean of 48.65 ± 17.33 years. IL-6 and IL-8 were measured using ELISA and G-CSF using the immunoassay technique at day 0 and after 48 hours. Culture from the site of any infection was done at day 0 and at any time during patient stay if severe signs of infection or septicemia developed. CBC, blood gases and chest X-ray, APACHE II score and MOSD were done daily.

**Results** Chest infection was the most common site of infection (48 patients, 60%), followed by mixed wound infection (10 patients, 12.5%) and abdominal sepsis (six patients, 7.5%), two patients with urosepsis (2.5%) and source of infection can found in four patients (5%).

A significant positive correlation was found between cytokine levels, the scoring systems and blood cultures in the four groups.

## P161

### Marker or mediator? Changes in endotoxin activity as a predictor of adverse outcomes in critical illness

**D Klein[1], A Derzko[2], A Seely[3], D Foster[2], J Marshall[1]**
*[1]University of Toronto, Canada; [2]Spectral Diagnostics, Toronto, Canada; [3]University of Ottawa, Canada*
*Critical Care* 2005, **9(Suppl 1):**P161 (DOI 10.1186/cc3224)

**Introduction** Endotoxin is a potent trigger of the inflammatory cascade in critical illness. We have previously shown that endotoxin activity levels (EAA) on admission to the ICU predict adverse clinical outcomes.

**Objective** To determine the significance of changes in EAA values over time in patients with critical illness.

**Methods** Data were extracted from the Multi-centre Endotoxin Detection in Critical Illness trial database for patients who had a minimum of three EAA values (consecutive or nonconsecutive) during the first four ICU days beginning on ICU admission along with associated clinical outcome data. Change in EAA over time was defined qualitatively as an inflection in the curve generated by plotting EAA values over time using the assumption of a normal biologic polynomial distribution. Patients were grouped based on having either zero, one, or two inflections in EAA over the 4-day study period. Infection status was defined by the results of bacteriologic cultures and subsequent Clinical Evaluation Committee adjudication. The primary outcome measure was organ dysfunction over time as defined by the area under the curve generated by plotting MODS score against time (MODS burden) calculated over a 4-day period (trapezoidal rule). Secondary outcomes included ICU and hospital mortality.

**Results** In a total of 345 patients, 28 patients had zero inflections, 215 had one inflection, and 102 had two inflections. MODS burden was significantly elevated in patients with two inflections (MODS burden = 486 ± 232 MODS hours) as compared with those with zero (MODS burden = 252 ± 214 MODS hours) or one inflection (MODS burden = 386 ± 206 MODS hours) ($P < 0.00001$, $P = 0.001$, respectively; three-way analysis of variance $P < 0.00001$).

**Table 1 (abstract P160)**

| | SIRS | Sepsis | Severe sepsis | Septic shock |
|---|---|---|---|---|
| IL-6 (pg/ml) | 168.48 ± 101.68 | 664.9.1 ± 281.67 | 1931.8 ± 458.4 | 3330.3 ± 726 |
| IL-8 (pg/ml) | 31.35 ± 8.17 | 75.68 ± 13.98 | 272.6 ± 65.5 | 390.6 ± 49.50 |
| IL-10 (pg/ml) | 121.6 ± 21.2 | 202.8 ± 61.9 | 470.9 ± 153.3 | 1070.7 ± 525.4 |
| G-CSF (pg/ml) | 36.22 ± 10.52 | 103.89 ± 26.99 | 173.9 ± 30.68 | 405.97 ± 77.2 |

**Table 2 (abstract P160)**

| | | | | | |
|---|---|---|---|---|---|
| IL-6 (pg/ml) | –ve blood culture | 605.82 ± 572.14 | IL-10 (pg/ml) | –ve blood culture | 201.18 ± 121.81 |
| | +ve blood culture | 2879.49 ± 1017.87 | | +ve blood culture | 897.35 ± 522.44 |
| IL-8 (pg/ml) | –ve blood culture | 86.42 ± 84.15 | G-CSF (pg/ml) | –ve blood culture | 83.07 ± 50.73 |
| | +ve blood culture | 344.07 ± 108.17 | | +ve blood culture | 338.9 ± 126.6 |

EAA variability was predictive of organ dysfunction (MODS burden) over time ($P < 0.00264$). MODS burden correlated with both ICU mortality ($P < 0.00001$) and hospital mortality ($P < 0.0001$). EAA variability was found to be independent of infection status ($P = 0.7915$). The number of EAA inflections were more predictive of outcome than the absolute EAA value calculated as the total endotoxin activity load over the 4-day period (AUC, trapezoidal rule) (univariate regressions, $P < 0.00001$, $P = 0.5440$, respectively). In a separate study of 15 normal healthy volunteers, EAA variability was shown to contain zero inflections in all subjects studied.

**Conclusions** These data suggest that increased variability in endotoxin activity is associated with worsening outcomes in the critically ill. Our assumption of a normal biologic polynomial distribution of endotoxin activity requires validation with more frequent EEA sampling. Further studies are warranted to assess whether the dynamic alteration of endotoxin activity may play an important role in the ongoing inflammatory response and organ dysfunction in the critically ill.

## P162

### Rates of agreement of endotoxin, procalcitonin and lactate in septic and non-septic critically ill patients

**D Foster[1], A Romaschin[2], A Derzko[1], P Walker[1]**
*[1]Spectral Diagnostics, Toronto, Canada; [2]University Health Network, Toronto, Canada*
*Critical Care* 2005, **9(Suppl 1):**P162 (DOI 10.1186/cc3225)

**Introduction** In contrast with many acute and severe diseases such as myocardial infarction, liver failure and renal failure, severe sepsis lacks a specific biomarker. A useful marker of severe sepsis will guide therapy by identifying which patients have the pathological process of interest.

**Objective** To compare the rates of agreement between PCT and lactate (LAC) assays with endotoxin levels in severely septic and non-septic critically ill patients.

**Methods** Data were collected from stored frozen plasma samples from a multicenter study evaluating the Endotoxin Activity (EAA) Assay [1]. We evaluated test samples based on the presence of clinical determination of severe sepsis where $n = 17$ had elevated EAA levels and $n = 7$ had low EAA levels. There were $n = 18$ from non-septic critically ill patients with low EAA values. We then performed PCT and lactate assays on the same samples by technicians who were blinded to EAA results and clinical diagnosis. Overall percent agreement (weighted kappa statistic): EAA vs PCT = 73.81% (0.462), EAA vs lactate = 40.5% (–0.247), lactate vs PCT = 42.9% (–0.183) The EAA correctly identified 17 of 24 severely septic patients, thus showing a positive agreement of 70.8%. The PCT and lactate assays correctly identified 15 and six patients, respectively. The positive agreement with the consensus definition of severe sepsis was 62.5% for PCT and 25% for lactate.

**Table 1**

| | PCT < 2.0 | PCT > 2.0 | LAC < 2.0 | LAC > 2.0 |
|---|---|---|---|---|
| EAA < 0.6 | 19 | 6 | 13 | 13 |
| EAA > 0.6 | 5 | 12 | 12 | 4 |
| LAC < 2.0 | 13 | 13 | | |
| LAC > 2.0 | 11 | 5 | | |

**Conclusions** Both PCT and endotoxin are elevated in patients with severe sepsis. The reported positive agreement with a clinical diagnosis of severe sepsis provides evidence of their value as a diagnostic marker. The poor positive agreement between lactate levels and the presence of severe sepsis suggests this marker may have other value such as for prognosis. Further study is required to evaluate each of these markers as a measure of response to therapy.

**Reference**

1. Marshall J, *et al.*: *J Infect Dis* 2004, **190:**527-534.

## P163

### Prevention of postoperative infectious complications with procalcitonin-controlled early postoperative administration of IgM-enriched immunoglobulin preparation in high-risk children with congenital heart diseases

**N Beloborodova, D Popov, K Schatalov, M Zelenikin, G Lobatchova**
*Bakoulev Scientific Center for Cardiovascular Surgery, Moscow, Russia*
*Critical Care* 2005, **9(Suppl 1):**P163 (DOI 10.1186/cc3226)

**Objectives** To evaluate the effectiveness of procalcitonin (PCT)-controlled use of IgM-enriched immunoglobulin preparation in high-risk children with congenital heart diseases after cardiac surgery with cardiopulmonary bypass (CPB).

**Methods** During January–July 2004, 31 consecutive high-risk pediatric patients were enrolled into the study. The age was 23 (19–30) months. Severe concomitant extracardiac pathologies were registered in 22 (71%) of cases; 21 (68%) patients had preceding cardiovascular operations. Patients who had PCT blood plasma levels above 2 ng/ml on the first day after surgery ($n = 28$) were randomized into two groups. These groups were comparable by severity of initial condition, age and CPB time. IgM-enriched immunoglobulin preparation (Pentaglobin; Biotest Pharma GmbH, Germany) was administrated to the patients in the study group ($n = 15$) in addition to standard treatment (first 3 days after surgery, 5 ml/kg each day). Patients in the control group ($n = 13$) received only standard treatment. PCT blood plasma concentrations were measured by immunoluminometric method (PCT LIA; BRAHMS Aktiengesellschaft GmbH, Germany). The data are shown as median and 25th and 75th percentiles. The data were compared by Mann–Whitney U test, $P < 0.05$ considered statistically significant. Postoperative infections rates were analyzed in studied groups.

**Results** None of the patients had exhibited any signs of infection before surgery. Patients with PCT blood plasma levels less than 2 ng/ml on the first day after surgery ($n = 3$) had a smooth postoperative period. PCT levels on the first day after surgery were significantly higher in the control group in comparison with the study group (7.77 [5.95–10.72] ng/ml and 3.60 [2.98–6.54] ng/ml, respectively; $P = 0.009$). Postoperatively 1/15 (6.7%) of patients in the study group and 5/13 (38.5%) of patients in the control group suffered from infectious complications (study group: urinary tract infection – one patient; control group: pneumonia – two patients, pneumonia and sepsis – one patient, peritonitis with multiorgan failure – one patient, urinary tract infection – one patient). The rate of postoperative infectious complications was significantly lower in the study group ($P = 0.03$). Two deaths in the control group occurred due to sepsis ($n = 1$) and peritonitis with multiorgan failure ($n = 1$).

**Conclusions** High PCT levels on the first day after surgery are associated with high rates of infectious complications. PCT monitoring allows one to select patients with systemic bacterial inflammation after CPB. Early (on the first day after surgery) administration of IgM-enriched immunoglobulin preparation effectively prevents infectious complications in these patients.

## P164

### Evaluation of procalcitonin as a diagnostic and prognostic marker in patients with sepsis, severe sepsis and septic shock associated with ventilator-associated pneumonia

**S Virtzili[1], D Zervakis[1], A Koronaios[1], P Alevizopoulou[1], A Flevari[1], A Kotanidou[1], V Kousoulas[2], H Giamarellou[2], C Roussos[1]**
*[1]ICU, Medical School, Athens University, Athens, Greece; [2]4th Department of Internal Medicine, Medical School, Athens University, Athens, Greece*
*Critical Care* 2005, **9(Suppl 1):**P164 (DOI 10.1186/cc3227)

**Objectives** Although the significance of procalcitonin (PCT) has been evaluated for general populations of patients with sepsis attributed to various infections, application as a marker of severity with both diagnostic and prognostic implications in patients with ventilator-associated pneumonia (VAP) has not been specifically studied.
**Methods** Serum samples were collected on the first, third, fifth and seventh days of symptoms from 68 patients with sepsis, severe sepsis/shock (ASCP/SCCM 1992) and VAP. APACHE II and SOFA scores were measured on the first day of the symptoms. Patients were followed-up for 28 days for overall survival. PCT was estimated in sera of patients by immunochemiluminometric assay.
**Results** Among 68 patients, 34 presented with sepsis, five with severe sepsis and 29 with septic shock. Mean age (years, ± standard deviation) was 57.86 ± 18.85; 48 patients were male and 20 female. APACHE II and SOFA (mean ± standard deviation) were 18.28 ± 6.11 and 7.64 ± 3.24, respectively. After 28 days of follow-up, 38 patients were alive and 21 have died. Mean PCT concentrations (ng/ml) on days 1, 3, 5 and 7 in patients with sepsis, severe sepsis and septic shock are presented in Table 1.
The mean ± standard error serum concentrations of PCT of survivors at days 1, 3, 5 and 7 were 0.71 ± 0.19, 0.45 ± 0.09, 0.35 ± 0.05 and 1.42 ± 1.04, respectively. Respective values in non-survivors were 1.83 ± 0.86 ($P$ = not significant compared with survivors), 2.63 ± 1.08 ($P$ = 0.05), 3.61 ± 1.33 ($P$ = not significant) and 2.89 ± 0.99 ($P$ = 0.02).

**Table 1**

**Mean procalcitonin concentrations (ng/ml)**

| | Day 1 | Day3 | Day 5 | Day 7 |
|---|---|---|---|---|
| Sepsis | 0.73 | 0.53 | 0.92 | 0.50 |
| Severe sepsis | 0.61 | 0.55 | 0.83 | 0.99 |
| Septic shock | 1.45 | 1.88 | 1.93 | 3.54 |

**Conclusions** PCT is a crucial marker of overall survival in patients with septic syndrome and VAP. This suggestion is further supported by the fact that PCT correlates to the severity of disease constituting an objective marker of sepsis.

## P165

### Changes in procalcitonin in septic shock patients treated with endotoxin adsorption therapy

**T Ikeda, K Ikeda, M Nagura, H Taniuchi, Y Kuroki, M Matsushita**
*Hachiouji Medical Center, Tokyo Medical University, Tokyo, Japan*
*Critical Care* 2005, **9(Suppl 1):**P165 (DOI 10.1186/cc3228)

**Introduction** The endotoxin adsorption method (PMX-DHP: Toray Industries, Inc., Tokyo, Japan) is used for treatment of patients with sepsis and septic shock primarily caused by Gram-negative infections in Japan. Procalcitonin (PCT) levels may be a good marker of infection and levels exceeding 10 ng/ml occur almost exclusively in severe sepsis. The aim of this study was to evaluate PMX-DHP for severe sepsis or septic shock patients according to PCT values. Patients were classified as a group in which PCT is higher than 10 ng/ml (H group) or a group in which PCT is lower than 10 ng/ml (L group).
**Patients and methods** This mode of blood purification is principally applied on direct hemoperfusion therapy. Sixty-seven patients (40 in H group, 27 in L group) were treated with PMX-DHP. Sepsis was diagnosed according to the criteria of the American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference Committee. The following parameters (tumor necrosis factor alpha, IL-6, IL-8, IL-1ra, ICAM-1, PAI-1 and PCT) were measured just before and immediately after PMX-DHP. PCT was measured by immunoluminometric assay (LUMI test PCT; BRAHMS Diagnostica, Berlin, Germany).
**Results** APACHE II score in the H group was 26.7 ± 7.6 and in the L group was 24.7 ± 9.2, respectively. SOFA score in the H group was 11.2 ± 3.8 and in the L group was 11.3 ± 4.2. The 28-day all-cause mortality rate in the H group was 30% and was 33% in the L group. These were no significant differences between the groups. IL-6, IL-8, and IL-1ra in H group were remarkably higher than in the L group. (Median IL-6, IL-8, and IL-1ra in H group were 7580 pg/ml, 646 pg/ml, 55,000 pg/ml, respectively, and in L group were 462 pg/ml, 40 pg/ml, 3650 pg/ml, respectively.) PCT in the H group showed a tendency to decline from 108 ± 120 ng/ml to 94 ± 98 ng/ml before and after PMX-DHP. Especially, PCT of the survival group in H group showed a significant decrease from 119 ± 138 ng/ml to 93 ± 102 ng/ml ($P < 0.02$). On the other hand, PCT of the nonsurvival group in H group increased from 83 ± 58 ng/ml to 96 ± 91 ng/ml.
**Discussion** Serum PCT values were less than 0.1 ng/ml in healthy individuals, but markedly increased, mostly due to extra-thyroid production in cases of severe infection. Recent findings suggest that sources of PCT may include liver cells and monocytes/macrophages. PCT is consistently increased after endotoxin injection, suggesting an association of endotoxin with septic shock and high PCT serum concentration.
**Conclusion** Our results may suggest that PMX-DHP can reduce various cytokines and serum PCT in the survival group.

## P166

### Procalcitonin guidance significantly reduces antibiotic duration in community-acquired pneumonia: the 'ProCAP' study

**M Christ-Crain, D Stolz, R Bingisser, C Mueller, J Leuppi, M Battegay, P Huber, M Tamm, B Mueller**
*University Hospital, Basel, Switzerland*
*Critical Care* 2005, **9(Suppl 1):**P166 (DOI 10.1186/cc3229)

**Background** Community-acquired pneumonia (CAP) is routinely treated with antibiotic courses of 10–14 days. Procalcitonin (ProCT) is elevated in systemic bacterial infections, but remains low in viral infections. Its potential as a tool to guide AB prescription in lower respiratory tract infections has been shown [1]. This study aims to evaluate ProCT stewardship to reduce AB duration in patients with CAP.
**Methods** From a prospective, single-blinded, randomized study, data of 200 patients with CAP were analyzed. The standard group ($n$ = 101) received antibiotics as generally recommended. In the ProCT group ($n$ = 99), ProCT levels were measured at days 4, 6 and 8 and antibiotic therapy was discontinued if levels were < 0.25 μg/l, measured with a sensitive assay (Kryptor PCT, BRAHMS, Germany). At baseline and at follow-up at 6 weeks, a standardized work-up was performed.

**Results** Baseline characteristics in both groups (Standard/ProCT) were similar (*P* values of quality of life score [41 ± 22/43 ± 21], temperature [38 ± 1/38 ± 1], leucocytes [13 ± 6/14 ± 7], C-reactive protein [160 ± 95/142 ± 120] and ProCT [median: 0.4/0.6] were not significant). Fifty-eight percent of patients had a high (class IV, V) pneumonia severity index. In the standard group, the mean duration of antibiotic therapy was 14.2 ± 7.3 days as compared with 6.2 ± 6.2 days in the ProCT group ($P < 0.001$). A total 99.5% of patients underwent a follow-up. There were no differences in clinical, radiographic and laboratory outcome data as well as in mortality (14.5%) between groups.

**Conclusions** The duration of antibiotic treatment in patients with CAP can be markedly and safely reduced using a ProCT-guided treatment algorithm, with similar outcome. In view of the increasing antimicrobial resistance and costs, these findings have important clinical implications.

**Reference**

1. Christ-Crain M, *et al.*: *Lancet* 2004, **363:**600-607.

## P167

### Predictive value of procalcitonin and IL-6 for postoperative sepsis

**G Marx[1], S Swaraj[2], A Breen[2], G Ritchie[2], A Shenkin[2], C Toh[2], M Leuwer[2]**

*[1]Friedrich-Schiller-University of Jena, Germany; [2]University of Liverpool, UK*

*Critical Care* 2005, **9(Suppl 1):**P167 (DOI 10.1186/cc3230)

**Objectives** Early recognition of sepsis is of particular interest, because this could expedite the initiation of early specific treatment and could potentially improve patient outcome. The aim of this study was to determine the value of procalcitonin (PCT), white blood cell count (WBC), IL-6, terminal complement complex (C5b-9) and C-reactive protein (CRP) in the prediction of postoperative sepsis.

**Methods** In a prospective clinical observational study 72 non-infected patients admitted postoperatively to an ICU who required > 24 hours ICU treatment were recruited. Blood samples were collected on the first, second, third, fifth, seventh and 10th day. Each patient was examined daily for signs and symptoms of infection. Values were given as median and interquartile range (IQR). Diagnostic accuracy of the parameter determined at study entry was expressed as the area under the receiver-operating curve (AUC).

**Results** Of 72 recruited patients 11 developed postoperative sepsis and 18 severe sepsis or septic shock. Infection was microbiology proven in 22 of 29 patients (76%). The patients enrolled had an age of 68 (21.5) years and an initial SOFA score of 5 (4). After 28 days, 12 patients had died, 60 were survivors.

**Table 1**

**Diagnostic performance of markers to predict sepsis on inclusion day**

| | PCT | IL-6 | C5b-9 | WBC | CRP |
|---|---|---|---|---|---|
| Cut-off value | 2 ng/ml | 150 pg/ml | 600 ng/ml | 12,000 $mm^{-3}$ | 150 mg/ml |
| Sensitivity (%) | 52 | 90 | 31 | 41 | 55 |
| Specificity (%) | 86 | 40 | 65 | 65 | 60 |
| AUC | 0.70* | 0.80* | 0.51 | 0.54 | 0.64 |

*$P < 0.05$.

**Conclusion** Our results indicate that in postoperative patients prior to the onset of any clinical deterioration PCT may be a specific predictive marker and IL-6 may be a sensitive predictive marker for sepsis.

**Acknowledgements** This study was supported by grants from the R&D RLBUH NHS Trust support fund and from the R&D fund of the University of Liverpool.

## P168

### Infections after myocardial infarction and cardiogenic shock and their reflection by inflammation parameters

**H Mitterhammer, K Smolle, G Baumann, W Wonisch, R Aigner, G Egger**

*University Hospital, Graz, Austria*

*Critical Care* 2005, **9(Suppl 1):**P168 (DOI 10.1186/cc3231)

**Objective** Cardiogenic shock shows a high incidence of infections. The preceding myocardial trauma and shock as well as bacterial infection may trigger an inflammatory response. We investigated whether different inflammation parameters can alternatively be related to myocardial trauma/shock versus infection.

**Patients** Fifteen patients (10 males/five females), mean age 69 ± 10.5 years and mean APACHE III score 83.36 ± 14.1, were enrolled in this prospective study. Cause of ICU admission was cardiogenic shock due to myocardial infarction (MI). Inclusion criteria were need of mechanical ventilation and vasopressor support. All patients developed respiratory tract infections and were treated with antibiotics.

**Methods** Measurements started on day 1 after MI and were performed daily until day 10. Polymorphonuclear leukocyte (PMN) functions were measured in fresh whole blood: PMN migration was measured with a membrane filter method under FMLP stimulation; ROS release with luminol-enhanced chemiluminescence under PMA stimulation. Blood levels of PMN elastase, PMN blood count, sL-selectin, IL-6, IL-10, PCT, CRP, neopterin; and the infarction-related and shock-related parameters Troponin T and lactate were measured with routine methods. Changes in the parameters over time were determined with linear regression of log *y*.

**Results** Among the parameters, three groups of reactivity emerged. Parameters of group I developed maximum reactions on days 1, 2 or 3 after MI, and values decreased significantly over the observation period. This group included PMN elastase, IL-6, PCT, Troponin T and lactate. Group II parameters developed maxima respectively minima on days 3, 4 and 5. This group included PMN-ROS release and neopterin (maxima), and PMN blood count and migration (minima). Parameters of group III showed maximum values on days 2 or 3, but no significant decrease (CRP and IL-10), or no distinct changes at all (sL-selectin). Infections appeared on day $X = 3.92 \pm 1.25$ standard deviation after MI. Thus, top values of group II parameters coincided with the onset of infection, while in group I high values followed immediately MI and shock.

**Conclusion** PMN-elastase, IL-6 and PCT parallel Troponin T and lactate can thus be considered to be triggered by myocardial trauma and shock. They are no indicators of infection. Blood PMN numbers, migration and ROS release as well as neopterin reached minimum/maximum values around the clinical manifestation of infection, suggesting associations with infections. Their decrease/increase may indicate the onset of infections.

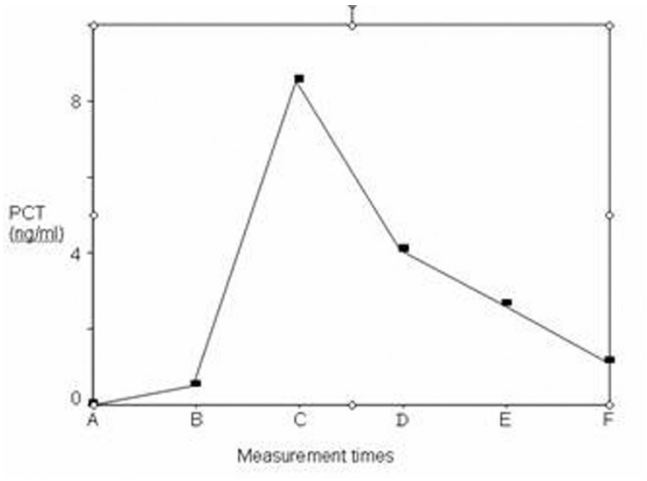
## P169

### Does cardiopulmonary bypass affect the procalcitonin level?

**F Kalay, Y Bicer, S Simsek, N Yapici, Z Alicikus, G Golcuklu, Z Aykac**
*Siyami Ersek Thoracic and Cardiovascular Surgery Center, Istanbul, Turkey*
Critical Care *2005,* ***9(Suppl 1):***P169 (DOI 10.1186/cc3232)

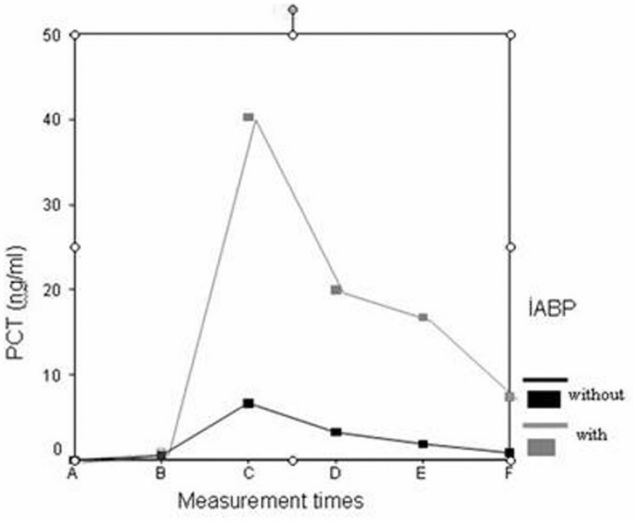
**Introduction** Cardiopulmonary bypass (CPB) causes an inflammatory response with clinical and biological changes. This systemic inflammatory response syndrome (SIRS) is a result of several stimuli such as exposure of blood to non-physiological surfaces, surgical trauma, myocardial ischaemia-reperfusion and endotoxin release. Because of this response, conventional clinical and biological signs may be misled in the diagnosis of postoperative complications, particularly infection. Procalcitonin (PCT) is useful as a marker of infection. Further studies suggested that PCT is an early, sensitive and specific indicator of infection but recent investigations showed increases in other conditions associated with systemic inflammation, such as severe trauma, burns and heat stroke. The aim of this study was to determine the normal profile of PCT during preoperative, peroperative and postoperative (PO) periods in patients undergoing cardiac surgery with cardiopulmonary bypass (CPB).
**Methods** We have measured serum PCT levels in 91 patients undergoing elective cardiac surgery with CPB. PCT levels were measured after induction of anaesthesia (baseline), after CPB and PO days 1, 2, 3 and 4. The demographic data of all patients, cross-clamping and bypass times, inotropic medication or intra-aortic balloon pump (IABP) needs were recorded. Repeated-measures analysis of variance was used for statistical analyses.
**Results** Baseline PCT levels were measured before the operation ($< 0.05$ ng/dl) and all increased at the end of the CPB. The increase in serum PCT levels had a peak on the first postoperative day ($P < 0.001$) (Fig. 1). PCT levels were higher in some patients whose cross-clamping and total bypass times were longer than others or they needed inotropic agents or IABP. Repeated variant analyses showed that there was a closed relationship between the PCT levels and cross-clamp and total bypass times, need of inotropic medications and IABP (Fig. 2).
**Conclusion** Although PCT is a useful marker of infection, it can be affected from many factors (CPB itself, prolonged operation, cross-clamping and bypass time, inotropic agent and IABP need, etc.) during CPB. So PCT alone is not enough to decide for infection in the early postoperative period in cardiac surgery patients.

**Figure 1 (abstract P169)**




The procalcitonin (PCT) levels and distribution of measurement times: A, baseline; B, after cardiopulmonary bypass; C, postoperative (PO) day 1; D, PO day 2; E, PO day 3; and F, PO day 4.

**Figure 2 (abstract P169)**




Procalcitonin (PCT) levels in patients with and without intra-aortic balloon pump (IABP).

## P170

### The prognostic value of procalcitonin in cardiac surgical patients

**C Iasonidou, G Vasiliadou, F Ampatzidou, N Manolakoglou, V Soulountzi, N Kapravelos**
*2nd Intensive Care Unit, Papanikolaou General Hospital, Thessaloniki, Greece*
*Critical Care* 2005, **9(Suppl 1):**P170 (DOI 10.1186/cc3233)

**Introduction** The aim of this prospective study was to determine the prognostic value of serum levels of procalcitonin (PCT) in patients early after cardiac surgery using cardiopulmonary bypass (CPB). We studied whether PCT is useful as an early prognostic marker in cardiosurgical patients with respect to complications and infections and whether PCT is a specific marker for the occurrence of infections.
**Methods** We studied 74 patients (mean ± standard deviation age, 65 ± 9) after elective cardiac surgery and daily until the second postoperative day. Demographic data, operative data and clinical endpoints (SIRS, infection and severe complication) were documented. Complications were defined as circulatory failure, respiratory failure, renal dysfunction, hepatic dysfunction, and coagulation dysfunction.
**Results** SIRS occurred in 46 patients (62%), infection in four patients (5.4%) and non-infectious complication in 35 patients (47.2%). Circulatory failure occurred in 29 patients, respiratory failure in 19 patients, renal failure in two patients, hepatic dysfunction in six patients, coagulation dysfunction in eight patients. Serum PCT concentrations increased in all patients with

peak levels occurring on the first postoperative day (PCT1: 0.495 standard error of the mean [SEM] 0.068, PCT2: 2.62 SEM 0.42, PCT3: 1.65 SEM 0.23). The serum PCT levels were increased in patients with SIRS compared with patients with no-SIRS. Using the Mann–Whitney U test we found a statistically significant increase on PCT levels in patients with infection ($P = 0.001$) and in patients with non-infectious complications ($P = 0.005$). PCT was not significantly different in patients with infectious complications in comparison with patients with non-infectious complications. There was good correlation (Pearson correlation) between PCT level and CPB duration, duration of aortic clamping and EURO score.

**Conclusion** PCT is a valuable prognostic marker early after cardiac surgery using CPB with respect to infection and severe complications. However, PCT does not differentiate infectious and non-infectious complications.

## P171

### The procalcitonin test in the evaluation of clinical severity in patients with acute pancreatitis

**B Gelfand, M Filimonov, S Burnevich, T Brazhnik, N Sergeyeva**
*The State Medical University of Russia, Moscow, Russia*
*Critical Care* 2005, **9(Suppl 1):**P171 (DOI 10.1186/cc3234)

**Purpose** To determine the role of the procalcitonin test in the clinical and laboratory evaluation of the clinical severity and the intensity of the systemic inflammatory reaction in patients with different forms of acute pancreatitis.

**Design** A prospective study.

**Patients** The study covered 50 patients with acute pancreatitis of various aetiologies. Patients were subdivided into five groups depending on morphological and microbiological criteria: (1) 10 patients with acute interstitial pancreatitis (AIP); (2) 16 non-operated patients with limited sterile pancreatic necrosis (LSN-N); (3) six operated patients with limited necrosis (LSN-O); (4) six patients with extensive sterile necrosis (ESN); (5) 12 patients with infected forms of pancreatic necrosis (IPN).

**Methods** Plasma procalcitonin (PCT) concentrations were determined using an immunoluminometric method. The clinical severity of the patients' condition was evaluated with the help of the integral APACHE II scale. Laboratory and instrumental techniques of investigation were supplemented by calculations of the leucocyte intoxication index.

**Results** The mean PCT concentration in infected forms of destructive pancreatitis was markedly higher than in acute interstitial pancreatitis or sterile pancreatic necrosis, at a level of 2.95 ± 0.84 ng/ml. The PCT concentration rose as the patient's condition became more severe, and as it evolved from an interstitial form to infected pancreatic necrosis. A direct correlation was established between the PCT concentration and the APACHE II score ($r = 0.56$). A PCT concentration $> 2$ ng/ml is a threshold level indicating infection of pancreatic tissue.

**Conclusions** The procalcitonin test is an objective criterion in the complex evaluation of clinical severity in patients with acute pancreatitis. Monitoring of the PCT concentration assists in the early diagnosis of infective complications of acute pancreatitis, and allows surgical and intensive-care treatment strategies to be optimised in these patients.

## P172

### Procalcitonin in the critically ill

**A Kazda[1], J Valenta[1], H Brodska[1], M Stritesky[1], Z Stach[1], J Hendl[2]**
*[1]University Hospital, Prague 2, Czech Republic; [2]Charles University, Prague, Czech Republic*
*Critical Care* 2005, **9(Suppl 1):**P172 (DOI 10.1186/cc3235)

**Aim** To evaluate the diagnostic significance of procalcitonin (PCT) in critically ill patients and to compare its changes with changes of other acute phase reactants.

**Methods** In 45 patients a total of 188 investigations of orosomucoid, alpha-1-antitrypsin, C-reactive protein (CRP), PCT, albumin, pre-albumin, cholinesterase, number of leukocytes, platelets, fibrinogen and indexed Quick's test (INR) were carried out. The investigations were repeated as requested by the clinical state. Also followed were the results of haemoculture, bacteriological investigations, the presence of the systemic inflammatory response syndrome (SIRS), frequency of sepsis, severe sepsis, septic shock and the number of organ failures. PCT was investigated by LUMItest-PCT-kit (BRAHMS Berlin, Germany), and other parameters by routine laboratory methods.

**Results** From all investigated acute phase reactants only PCT and CRP offered the highest diagnostic and differentially diagnostic value. Therefore only these two parameters are presented in the following survey together with the number of leukocytes and temperature. Based on the criterion of the presence of apparent infection (no:yes [134:50 findings]) and positivity of bacteriological cultivation (no:yes [42:143]), there was a significant difference in PCT and temperature, but not in CRP or number of leukocytes. As for haemoculture positivity (no:yes [169:16]), a significant difference was only found for the temperature. For the presence of SIRS (no:yes [52:142]), the differences were significant for PCT, CRP, as well as for temperature and leukocytes.

MODS was divided according to the number of affected organs into categories 1–4 (number of findings 47:56:63:12).The found values: PCT (ng/ml) 0.9 ± 1.9, 1.4 ± 2, 3.2 ± 4.4 and 7.5 ± 5.9, and CRP (mg/l) 108 ± 65, 195 ± 129, 191 ± 165 and 130 ± 62. Out of all findings, 36 were classified as sepsis, 50 as severe sepsis and 48 as septic shock. In following the order parameter, its value in sepsis, severe sepsis and septic shock is presented. The significance of differences on the 1% level is marked; it is for sepsis:severe sepsis +, for sepsis:septic shock ++ and for severe sepsis:septic shock +++; on the 5% level the same symbols are in parentheses. Leukocytes ($10^9$/l): 11.8 ± 4.9, 16.0 ± 7.6, 13.9 ± 8.8 (+, ++). CRP (mg/l): 128 ± 86, 191 ± 148, 204 ± 155 ([+], ++). PCT (ng/ml): 1.26 ± 2.31, 4.06 ± 6.46, 6.35 ± 11.91 (+, ++). Temperature (°C): 38.3 ± 0.7, 38.5 ± 0.8, 39.0 ± 1.2 (+, ++, +++).

**Conclusion** PCT helps to distinguish the gravity of the patient's state as shown by different values in sepsis and severe sepsis or by its relations to MODS. The investigation of PCT is demanded for more accurate diagnosis of infected patients and in case of discrepancy between the clinical state and CRP.

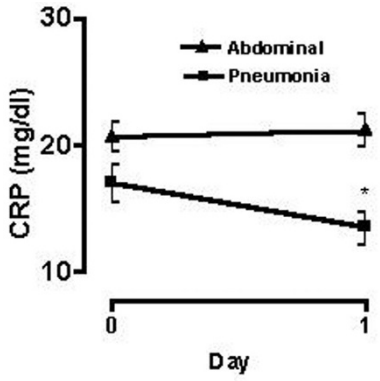
## P173

### Serum C-reactive protein levels in patients with sepsis varies according to the site of infection

**S Lobo, E Higashiama, D Rezende Jr, E Sivieiro, L Sanches**
*Famerp – Hospital de Base, Sao José do Rio Preto, Brazil*
*Critical Care* 2005, **9(Suppl 1):**P173 (DOI 10.1186/cc3236)

**Introduction** C-reactive protein (CRP) is a marker of inflammation used to monitor the course of infection and inflammatory diseases.

**Figure 1 (abstract P173)**




In critically ill patients the presence of several confounding factors very frequently covers up the site of infection. We aimed to investigate whether serum CRP levels vary according to the site of infection.

**Methods** Patients with sepsis, severe sepsis or septic shock were included. Serum C-reactive protein was measured within the first hours of ICU admission and day 1. Patients were classified according to the site of infection.

**Results** One hundred and fifty-eight patients with sepsis, severe sepsis and septic shock were included. Main sites of infection were abdominal in 44.3%, the lungs in 39.8%, the urinary tract in 8.2% and the bloodstream in 3.8%. Median levels of serum CRP on day 1 were 11.2 mg/dl, 14.3 mg/dl, 15.9 mg/dl and 20.3 mg/dl, for the lungs, bloodstream, urinary tract and abdominal, respectively. On day 1, CRP levels in patients with abdominal sepsis were significantly higher than in those with pneumonia-induced sepsis (21.6 ± 10.7 mg/dl vs 13.6 ± 10.3 mg/dl, $P < 0.05$).

**Conclusion** Serum CRP concentrations are higher in patients with abdominal sepsis than in patients with pneumonia induced-sepsis.

### P174

### C-reactive protein as a marker of septic shock and outcome in the intensive care unit

**M Theodorakopoulou[1], N Skabas[2], M Lignos[1], A Kandili[2], S Ioannidou[2], E Kavadia[2], A Armaganidis[1]**

*[1]Attiko University Hospital, Athens, Greece; [2]3rd Hospital of Ika, Athens, Greece*

*Critical Care* 2005, **9(Suppl 1):**P174 (DOI 10.1186/cc3237)

**Introduction** As an acute phase protein C-reactive protein (CRP) is directly related to the inflammatory response and it has been used to monitor the course of infection. The association of CRP levels and septic shock are not known. In this study we will examine the relationship of CRP levels to septic shock and to the outcome.

**Methods** A prospective study on a six-bed ICU of a university hospital and on a five-bed medical ICU of a tertiary care hospital. Data were collected prospectively over a period of 1.5 years. Sixty-eight patients were included in the study. Patient that stayed in the ICU for less than 5 days were excluded from the study, as well as patients that had infection at the time of admission. CRP, APACHE II score, SOFA, WBC, platelets and use of inotropes were recorded on days 1, 3, 6, 9, 12 and 15. Patients were followed up for a septic episode up to day 15 and were followed up to their discharge for outcome. All patients that were included in the study met the ACCP/SCCM consensus criteria for sepsis and septic shock. Serum CRP levels are expressed as mean ± standard deviation.

**Results** The group of patients were divided into septic ($n = 28$) and nonseptic ($n = 40$). Septic shock showed a strong relationship to CRP levels. Twenty-eight patients (41%) developed septic shock and all these patients had significantly higher CRP levels not only upon admission (13.3 ± 8.9 mg/dl vs 5.2 ± 7.1 mg/dl), but the high values persisted the following days as well. The overall mortality rate was (27.8%). Nonsurvivors had significantly higher CRP levels than survivors. Patients that showed further increase of CRP on day 3 showed a higher mortality rate (64%) when compared with patients that showed a reduction of CRP on day 3 (22%) and remained low. CRP values that remained high (>15 mg/dl) after day 9 were associated with an even higher incidence of death (72%). APACHE II and SOFA scores, leucocyte count and platelets showed no significant relationship to CRP on either groups. Furthermore, APACHE II and SOFA scores were similar for both groups upon admission.

**Conclusions** In our ICU elevated CRP values upon admission correlate strongly with increased risk of death. Persistently high CRP values correlate with even poorer outcome. Moreover, CRP is a good marker of septic shock. Overall, persistently high CRP values are associated with longer stay in the ICU, with septic shock, and with higher mortality. Since CRP seems to be a marker of an ongoing inflammatory process, then following the trends of such a marker might help in decision-making for further interventions on septic patients.

### P175

### Serial changes in soluble triggering receptor expressed on myeloid cells in the lung during ventilator-associated pneumonia

**R Determann[1], J Millo[2], S Gibot[3], M Vroom[1], C Garrard[2], M Schultz[1]**

*[1]Academic Medical Center, Amsterdam, The Netherlands; [2]John Radcliffe Hospital, Oxford, UK; [3]Réanimaton Medicale, Nancy, France*

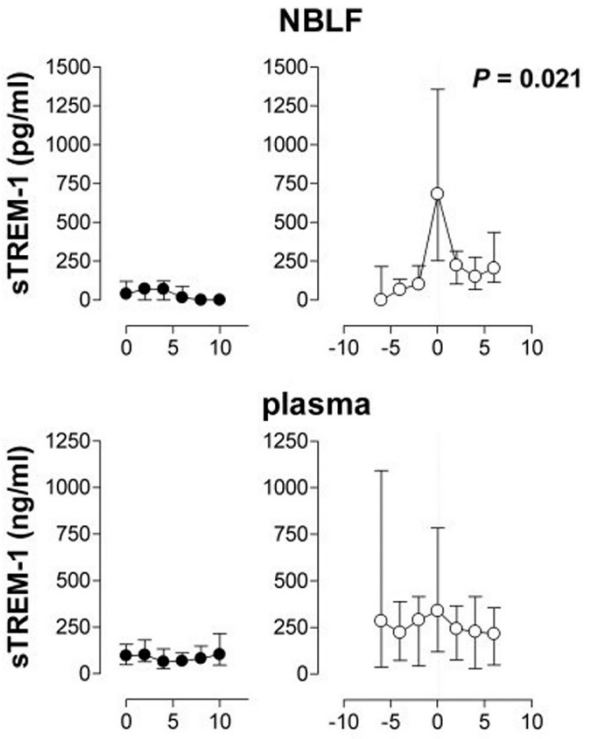
*Critical Care* 2005, **9(Suppl 1):**P175 (DOI 10.1186/cc3238)

**Introduction** The diagnosis of ventilator-associated pneumonia (VAP) remains a clinical challenge. Biological markers may facilitate the diagnosis of VAP. The triggering receptor expressed on myeloid cells (TREM-1) is a member of the immunoglobulin superfamily and is upregulated on phagocytes in the presence of bacterial products. Soluble (s) TREM-1 in bronchoalveolar-lavage fluid has been shown to be a promising biological marker for pneumonia. In the present study we performed serial measurements of sTREM-1 in lungs and plasma of patients who were at risk of developing VAP.

**Methods** In a single-centre prospective study, a non-directed bronchial lavage (NBL) was performed on alternate days in patients expected to require mechanical ventilation for > 5 days. A total of 28 patients were studied, nine of whom developed VAP. Diagnosis of pneumonia required a combination of clinical features plus microbiological confirmation. Levels of sTREM-1 were measured in NBL fluid (NBLF) and matching plasma samples by ELISA. Data are presented as medians (± IQR). Changes over time were tested within each group separately using analysis of repeated measures (linear mixed models). The *P* value in Fig. 1 denotes statistical significance.

**Results** Levels of sTREM-1 in NBLF (upper graphs) and plasma (lower graphs) of patients without VAP (left graphs) and of patients developing VAP (right graphs). In the first patient group 'day 0'

**Figure 1 (abstract P175)**




represents the day at which mechanical ventilation was initiated, in the latter group 'day 0' denotes the day at which the diagnosis of VAP was made clinically. The *P* value indicates statistical significance of rise of local sTREM-1 levels.

**Conclusion** NBLF sTREM-1 levels significantly rise in ventilated patients developing VAP. These results further confirm the usefulness of sTREM-1 as a biological marker for VAP.

## P176

## High mobility group box 1: as a 'testament' mediator

**I Maruyama[1], K Abeyama[1], T Ito[1], KK Biswas[1], K Kawahara[1], T Hashiguchi[1], K Yakabe[2], S Yamada[2], H Wada[3]**

*[1]Department of Laboratory and Molecular Medicine, Faculty of Medicine, Kagoshima University, Kagoshima, Japan; [2]Central Institute, Shino-Test Corporation, Kanagawa, Japan; [3]Mie University, Mie, Japan*

*Critical Care* 2005, **9(Suppl 1):**P176 (DOI 10.1186/cc3239)

**Introduction** In general, cells responded to stresses by the following hierarchy: (1) stored mediator release reaction phase (e.g. serotonin, histamine); (2) lipid mediator generation/release phase (e.g. PGs, LTs, endocannabinoids); (3) genomic reaction phase (e.g. self-defensive protein generation phase through NF-κB, AP-1 activation). As the last response, we propose (4) high mobility group box 1 (HMGB1) releases from necrotic cells.

In this study we present intracellular and intercellular dynamics of HMGB1, and their roles in the pathogenesis in inflammation and organ failures.

**Methods and results** We developed a specific and sensitive HMGB1 assay by the ELISA method as presented elsewhere in this congress (Yakabe K, *et al*., P177). Using this assay method, we evaluated serum HMGB1 levels in patients with various diseases. As a whole, the HMGB1 concentrations were elevated in various diseases that were correlated to the severity of organic cellular damages. These include infections, trauma, surgical operations, malignancies, and so on. The marked increase of HMGB1 (>10 ng/ml) was suggestive of presence of severe organ damages. However, the increased level of HMGB1 was not always sustained at higher levels and resultant lethality – because in some cases we observed that the elevated levels of HMGB1 rapidly decreased to subnormal or normal ranges with resulting recovery of the illness. This result suggested the presence of degrading or clearance mechanism of the protein. Thus, we examined the fate of the increased level of HMGB1 in the circulation.

At present, we have identified at least three pathways to decrease as well as produce the clearance of the circulatory HMGB1. The first is the degradation of HMGB1 by plasmin. We found that plasmin efficiently degraded HMGB1. The second way is the endothelial-dependent HMGB1 degradation by protein 'X'. HMGB1 binds to endothelium and be degraded by 'X'. The third way is the binding of HMGB1 by specific binding sites on diverse cells. These may include RAGE and proteoglycans. By these three routes, HMGB1 may be efficiently sequestered from the circulation and localized and enriched to the damaged tissue. The HMGB1 *in situ* acted as a stem cell inducer resulting in repair of damaged tissue/organ.

**Discussion** HMGB1 is released from most necrotic cells and behaves as a 'testament' mediator because this protein may be released in necrotic tissues including infection, injury and so on. The localized HMGB1 may act as an immune adjuvant and stem cell chemoatractant as recently described, and may play an important role for self-defense and repair of damaged tissue. However, if the HMGB1 released in cellular necrotic lesions entered into the circulation, this may diffuse the inflammation, and result in 'metastasis' of inflammation and organ failures. Therefore, HMGB1 should be enriched in injury sites, inhibiting its diffusion. We propose that this HMGB1 sequestering system is composed of plasmin, syndecan and endothelium. When this HMGB1-sequestering system is impaired, HMGB1 will enter into the circulation and act as a mediator of organ failure.

## P177

## High mobility group box 1 (HMGB1) quantified by ELISA that dose not cross-react with HMGB2

**K Yakabe[1], S Yamada[1], M Kobayashi[2], I Maruyama[3]**

*[1]Shino-Test Corporation, Kanagawa, Japan; [2]Hyogo Emergency Medical Center, Hyogo, Japan; [3]Department of Laboratory and Molecular Medicine, Faculty of Medicine, Kagoshima University, Kagoshima, Japan*

*Critical Care* 2005, **9(Suppl 1):**P177 (DOI 10.1186/cc3240)

**Introduction** Recently, high mobility group box 1 (HMGB1) was identified as a late mediator of endotoxin lethality. Patients with sepsis who succumbed to infection had increased serum HMGB1. However, it revealed that HMGB1 and HMGB2, with extremely high homology (81%) to HMGB1, coexist in the serum. We report an ELISA method we have developed that measured only HMGB1 without simultaneous determination of HMGB2.

**Methods** We developed anti-HMGB1 polyclonal and anti-HMGB1, 2 monoclonal antibody. We checked that developed antibodies both cross-reacted with porcine, bovine, rabbit, rat and mouse HMGB1 by western blotting because of more than 98% identity in amino acid sequence between these kinds and human. Using these antibodies, we developed a sandwich ELISA method

to measure HMGB1 specifically but be insensitive to HMGB2 in human serum. Using this method, we measured HMGB1 in samples obtained from 44 patients with septic shock and examined the following: (1) the participation of HMGB1 in septic shock, (2) the correlation of cytokines and HMGB1 in septic shock, and (3) the correlation of HMGB1 level and the therapeutic effect of endotoxin adsorption therapy (PMX-DHP).

**Results** With this method, the detection limit was 1 and 0.3 ng/ml, respectively, using the chromogenic substrate TMBZ and the chemoluminescent substrate PS-atto. This assay system showed 85–108% recovery by external addition recovery test. (1) The HMGB1 concentration in serum was significantly higher in the septic shock death group than the survival group. In addition, there appeared to be a positive correlation between serum HMGB1 concentration and SOFA score. (2) A negative correlation was observed between serum HMGB1 and cytokine concentration. (3) The HMGB1 concentration in serum decreased after PMX-DHP in all cases. In particular, the serum concentration decreased significantly after PMX-DHP in the survival group.

**Discussion** Using our assay method, HMGB1 was detected in the blood of patients with septic shock. The results suggested that HMGB1 plays an important role in aggravation of the condition in septic multiple organ failure.

## P178

## High-mobility group box 1: role in ARDS

**A Ishizaka[1], S Hashimoto[2]**
*[1]Keio University School of Medicine, Tokyo, Japan; [2]Kyoto Prefectural University of Medicine, Kyoto, Japan*
*Critical Care* 2005, **9(Suppl 1):**P178 (DOI 10.1186/cc3241)

Extracellular high-mobility group box 1 (HMGB-1), first isolated approximately 30 years ago from the thymus as a chromosomal protein and recognized as a transcriptional factor, has recently been proposed as one of the late mediators of sepsis and lipopolysaccharide (LPS) endotoxin acute lung injury (ALI) [1,2]. In recent studies, HMGB-1 has been implicated in the development of arthritis, activation of human monocytes, smooth muscle cell chemotaxis, and induction of adhesion molecules in endothelial cells. These observations suggest that HMGB-1 is a key mediator of cell injury, and that its inhibition may be key in improving clinical outcomes. We conducted a translational study to examine the participation of HMGB-1 in the pathogenesis of ALI caused by sepsis. To test the hypothesis that HMGB-1 plays a key role as a late mediator, we first measured its concentrations and those of its related compound, HMGB-2, in the blood and lungs of patients presenting with septic ALI/ARDS, and in a murine model of LPS-induced lung injury. We then studied the localization of the extracellular HMGB-1 protein and examined the anti-inflammatory effects of anti-HMGB-1 antibodies in our LPS-induced lung injury murine model. The direct effects of HMGB-1 and HMGB-2 on the lung were also examined. This study was performed to examine the putative role of HMGB protein in the pathogenesis of ALI. Observations were made (1) in 21 septic patients with ALI and 15 patients with normal lung function, and (2) in a mouse model, 24 hours after intratracheal instillation of lipopolysaccharide. The concentrations of HMGB-1 were increased in plasma and lung epithelial lining fluid of patients with ALI and mice instilled with LPS. LPS-induced ALI was mitigated by anti-HMGB-1 antibody. Although this protein was not detected in the plasma of control humans or mice, the concentrations of HMGB-1 in lung epithelial lining fluid or in bronchoalveolar lavage fluid were unexpectedly high. The nuclear expression of HMGB-1 was apparent in epithelial cells surrounding terminal bronchioles in normal mice, while its nuclear and cytoplasmic expression was observed in alveolar macrophages in LPS-instilled mice. Lung instillation of HMGB-2 did not cause as much inflammation as HMGB-1. Extracellular HMGB-1 may play a key role in the pathogenesis of clinical and experimental ALI. However, its expression in normal airways is noteworthy, and suggests that it also plays a physiologic role in the lung.

**References**

1. Wang H, Bloom O, Zhang M, Vishnubhakat JM, Ombrellino M, Che J, Frazier A, Yang H, Ivanova S, Borovikova L, *et al.*: **HMG-1 as a late mediator of endotoxin lethality in mice.** *Science* 1999, **285:**248-251.
2. Abraham E, Arcaroli J, Carmody A, Wang H, Tracey KJ: **HMG-1 as a mediator of acute lung inflammation.** *J Immunol* 2000, **165:**2950-2954.

## P179

## Effect of dexamethasone on the myocardial expression of cytokines and heat shock proteins in human neonates

**E Wehage[1], M Qing[1], P Tassani[2], F Haas[2], J Hess[2], M Seghaye[1]**
*[1]Pediatric Cardiology, Aachen University of Technology, Aachen, Germany; [2]Department of Pediatric Cardiology, German Heart Centre at the Technical University Munich, Germany*
*Critical Care* 2005, **9(Suppl 1):**P179 (DOI 10.1186/cc3242)

**Background and aim** Cardiac surgery with cardiopulmonary bypass (CPB) stimulates the synthesis of the proinflammatory cytokines such as tumor necrosis factor alpha (TNF-$\alpha$), IL-6, IL-8, and anti-inflammatory cytokines such as IL-10. This study was intended to analyze the effect of preoperative administration of dexamethasone on gene expression of proinflammatory and antiinflammatory cytokines and heat shock protein in the myocardium.

**Methods** Neonates ($n = 22$) scheduled for arterial switch operation were double-blinded randomized to receive dexamethasone ($n = 11$) (1 mg/kg) or saline ($n = 11$) given intravenously 2 hours before induction of anesthesia. Biopsies were taken from the right atrial appendage immediately before initiation of CPB. Myocardial gene expression and synthesis of TNF-$\alpha$, IL-1$\beta$, IL-6, IL-8, IL-10, and of heat shock proteins HSP32, HSP90, and HSP70 were detected by quantitative real-time RT-PCR and by western blot.

**Results** Proinflammatory and anti-inflammatory cytokines as well as HSPs were expressed at the mRNA level. IL-6 and HSP70 were also expressed at the protein level. Expression of mRNA encoding for TNF-$\alpha$, IL-1$\beta$, IL-6, IL-8, IL-10, and HSP32 were lower in neonates treated with dexamethasone than in the others. In contrast, expression of HSP70 mRNA and for HSP90 mRNA and protein levels of IL-6 and HSP70 were not different between both groups.

**Conclusion** Our study shows for the first time expression of proinflammatory and antiinflammatory cytokines and of HSPs in the myocardium of human neonates undergoing cardiac surgery. Dexamethasone given before cardiac surgery is associated with a reduction of cytokine expression at induction of CPB. This might provide myocardial protection.

## P180

## Pretreatment of dexamethasone before cardiopulmonary bypass upregulates intrahepatic synthesis of IL-10 via the transcription factors Sp1 and Sp3 and CCAAT/enhancer-binding protein

**Q Ma, M Wöltje, K Schumacher, M Sokalska, J Vazquez-Jimenez, M Seghaye**
*Klinik fur Kinderkardiologie, Aachen, Germany*
*Critical Care* 2005, **9(Suppl 1):**P180 (DOI 10.1186/cc3243)

**Background and aim** IL-10 is an anti-inflammatory cytokine produced by a variety of cell types including Kuffper cells and

hepatocytes. A recent study showed that IL-10 gene expression induced by endotoxin (LPS) in mouse macrophages is controlled by the cooperation of the promoter-selective transcription factors (Sp)1 and Sp-3 as well as by CCAAT/enhancer-binding protein β (C/EBPβ). Dexamethasone (Dex) has been recommended during cardiac surgery since it increases blood IL-10 levels during cardiopulmonary bypass (CPB) and reduces the release of proinflammatory mediators including tumor necrosis factor alpha. In an experimental model of cardiac surgery, it reduces the production of iNOS and COX-2.

This study was designed to identify the signaling pathways involved in intrahepatic overexpression of IL-10 induced by pretreatement by Dex before CPB.

**Methods** Animals were treated with Dex (1 mg/kg) ($n = 9$) or with saline ($n = 6$) given intervenously before normothermic CPB. Samples of liver tissue were taken before and 6 hours after CPB. IL-10 mRNA was assessed by competitive RT-PCR. Protein levels of IL-10, iNOS and COX-2 were assessed by western blot. Phosphorylation of extracellular regulating kinase (ERK1/2) and of the inhibitory protein of NF-κB (IkB) as well as nuclear protein levels of C/EBPβ were also detected by western blot. Activation of Sp1 and Sp3, C/EBPβ, NF-κB, and AP-1 were assessed by electrophoretic mobility shift assay with supershift. Liver tissue damage score was assessed by standard histology.

**Results** Pigs treated with Dex showed significantly higher intrahepatic concentration of IL-10 and lower concentrations of iNOS and COX-2 than the others. The former also showed lower tissue damage score. This upregulation of IL-10 and downregulation of iNOS and COX-2 observed in the treated group was associated with a higher activation of Sp1 and Sp3 as well as C/EBPβ. Moreover, levels of phospho-ERK1/2 and of C/EBPβ in nuclear extract were significantly higher 6 hours after CPB in pigs treated with Dex than in the others. Activation of NF-κB and of activator protein-1 was not significantly different between both groups.

**Conclusion** Our results show for the first time that Dex administration prior to CPB upregulates IL-10 via Sp1 and Sp3 as well as throughout C/EBPβ activation. This leads to attenuation of expression of iNOS and COX-2 and to hepatic protection.

## P181

### Moderate hypothermia during cardiopulmonary bypass reduces intramyocardial expression of tumor necrosis factor alpha via inhibition of AP-1

**Q Ma[1], M Wöltje[1], K Schumacher[1], M Sokalska[1], J Vazquez-Jimenez[2], E Wehage[1], M Seghaye[1]**
*[1]klinik fur Kinderkardiologie, Aachen, Germany; [2]Pediatric Cardiology, Aachen University of Technology, Aachen, Germany*
*Critical Care* 2005, **9(Suppl 1):**P181 (DOI 10.1186/cc3244)

**Background and aim** Moderate hypothermia during CPB inhibits intramyocardial tumor necrosis factor alpha (TNF-α) synthesis. Since the expression of TNF-α and other inflammatory mediators such as cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) is regulated by the NF-κB and activator protein (AP)-1 pathways, this study was intended to analyze the effect of moderate hypothermia during CPB on these signaling pathways in the myocardium.

**Methods** Twelve young pigs were randomly mounted on standardized CPB in moderate hypothermia or normothermia (temperature 28°C or 37°C, respectively, $n = 6$ each group). Myocardial probes were sampled from the right ventricle before, during and 6 hours after CPB. Messenger RNA encoding for TNF-α was assessed by competitive RT-PCR. Protein levels of TNF-α, iNOS, and COX-2 were assessed by western blot. Activation of NF-κB and phosphorylation of its inhibitory protein IkBa, activation of AP-1 and phosphorylation of its complex c-Jun as well as of mitogen-activated protein kinase (MAPK) p38 were assessed by electrophoretic mobility shift assay with supershift and/or western blot, respectively.

**Results** Both TNF-α mRNA and TNF-α protein were detected as soon as 30 min after initiation of bypass in both groups. At that time, expression of TNF-α mRNA and protein levels tended to be lower in pigs operated on under moderate hypothermia than those operated on under normothermia ($P < 0.1$, respectively). Moreover, pigs operated on under moderate hypothermia showed lower expression of TNF-α mRNA and protein levels that the others 6 hours after CPB ($P < 0.05$, respectively). The course of the expression of COX-2 but not that of iNOS during and after CPB paralleled that of TNF-α. The activation of p38 MAPK and of its downstream effector AP-1 was lower in animals operated on in hypothermia than in the others ($P < 0.05$, respectively). In contrast, phosphorylation of IkB and NF-κB activity were similar in both groups.

**Conclusion** This study shows that the inhibition of the intramyocardial expression of TNF-α and of its secondary mediator COX-2 related to moderate hypothermia during CPB is associated with the inhibition of p38 MAPK–AP-1, but not of the NF-κB pathway.

## P182

### Prototype reagents for an automated serum inducible nitric oxide synthase assay

**S Roberts[1], D Binger[1], C Knott[2], C Evans[2], H Linton[2], K Marker[2], S Mikolajczyk[2]**
*[1]Beckman Coulter Inc., Chaska, MN, USA; [2]Beckman Coulter, Inc., San Diego, CA, USA*
*Critical Care* 2005, **9(Suppl 1):**P182 (DOI 10.1186/cc3245)

**Introduction** Recent reports indicate that inducible nitric oxide synthase (iNOS) can be detected in the serum of sepsis patients. In order to study the potential clinical utility of iNOS, both an analytical mass standard and an automated, specific immunoassay have been developed. A subcloned cell-line derived from DLD-1 cells has been developed that can be induced to express high levels of human iNOS. A prototype Access®-based immunoassay has also been developed.

**Methods** DLD-1-5B2 mammalian cells were grown in tissue culture using DMEM + 10% FCIII media. Cells were grown to confluency and changed to induction media containing DMEM plus interferon gamma, IL-1β and tumor necrosis factor alpha. Following induction, cells were incubated in 5% $CO_2$ at 37°C for 18–30 hours. INOS expression was evaluated with the prototype immunoassay consisting of dual iNOS-specific monoclonal antibodies and by production of nitric oxide (NO) as determined by nitrite detection using the Griess assay. iNOS was extracted from induced DLD-1 cells by freeze–thaw disruption.

**Results** Production of NO was not detected by the Griess assay until 10 hours after induction. The production of NO increased proportionally from 2.6 μM NO at 10 hours to 18.7 μM at 30 hours. Using the prototype immunoassay, iNOS was detected in cell extracts at 2 hours after induction at a concentration of 2.4 ng per $10^6$ cells. Levels increased steadily until reaching a plateau of approximately 150 ng per 106 cells from 18 to 30 hours. While the iNOS immunoassay was much more sensitive in detecting the early stages of iNOS induction than the measurement of NO production, the increase in iNOS expression was proportional to NO production over the first 18 hours post induction, once NO became measurable.

**Summary** DLD-1-5B2 cells can provide a stable source of human iNOS. NO production is proportional to mass of iNOS produced up to 18 hours in confluent, induced cells. Nominal values of iNOS detected by immunoassay were based upon calibration with commercial murine iNOS standards. Additional work is required to optimize the prototype for clinical use. Purification, characterization, and analytical mass assignment of iNOS from DLD-1-5B2 cells are in progress to provide mass standardization for the iNOS immunoassay.

**P183**

## Oxygen metabolism as an indicator in criteria for hemoperfusion using a polymyxin-B immobilized column introduction

**H Kushi[1], H Shoji[2], T Miki[1], J Nakahara[1], K Okamoto[1], T Saito[1], K Tanjo[1]**
*[1]Department of Emergency and Critical Care Medicine, Nihon University School of Medicine, Tokyo, Japan; [2]Toray Medical Co. Ltd, Tokyo, Japan*
*Critical Care* 2005, **9(Suppl 1):**P183 (DOI 10.1186/cc3246)

**Introduction** It has been reported that hemoperfusion with a column of polymyxin B immobilized on fibers (PMX-DHP) ameliorates hyperdynamic circulation in septic shock and improves survival rate. However, a variety of criteria for the introduction of PMX-DHP in sepsis patients are used by a number of facilities, standard criteria have yet to be established. We introduced PMX-DHP using oxygen metabolism as an indicator, and evaluated the effectiveness.
**Subjects and methods** Subjects consisted of 24 sepsis patients (19 men and five women; mean age 60 ± 15.4 years) who had undergone PMX-DHP between January 2003 and October 2004. A thermodilution catheter was inserted into all patients. Mixed venous oxygen saturation ($SvO_2$), oxygen delivery index ($DO_2I$), oxygen consumption index ($VO_2I$), and oxygen extraction ratio ($O_2ER$) were used as indicators of systemic oxygen metabolism, and the $PCO_2$ gap (gastric submucosal carbon dioxide partial pressure minus the partial pressure of carbon dioxide in arterial blood) measured by gastric air tonometry was used as the indicator of tissue oxygen metabolism. These parameters were measured before and 24, 48, 72, and 120 hours after PMX-DHP introduction. The severity of infection was evaluated by the Acute Physiology and Chronic Health Evaluation (APACHE) score.
**Results** Life expectancy: 18 patients survived; six died. APACHE scores of survivors and non-survivors were 22 ± 4.0 and 24 ± 3.5, respectively. There was no significant difference. In the survivors $SvO_2$, $DO_2I$, $VO_2I$, and $O_2ER$ had shifted to the normal range prior to treatment. Pretreatment, the $PCO_2$ gap was 17 ± 3.6 mmHg in these patients, who presented markedly dysfunctional tissue oxygen metabolism. However, this decreased over time, and at 120 hours after treatment the $PCO_2$ gap had decreased significantly, improving to values in the normal range. On the other hand, the non-survivors also presented high $PCO_2$ gap levels before treatment, similar to the survivors. Although $DO_2I$ was within the normal range, $VO_2I$ and $O_2ER$ were lower than normal.
**Conclusion** Although dysfunctional tissue oxygen metabolism occurred in both the survivors and non-survivors, non-survivors also presented dysfunctional systemic oxygen intake. These results suggest that early-stage introduction of PMX-DHP is desirable, when systemic oxygen metabolism is stable.

**P184**

## Early introduction of hemoperfusion with an immobilized polymyxin B fiber column eliminates humoral mediators and improves pulmonary oxygenation

**H Kushi[1], H Shoji[2], T Miki[1], J Nakahara[1], K Okamoto[1], T Saito[1], K Tanjo[1]**
*[1]Department of Emergency and Critical Care Medicine, Nihon University School of Medicine, Tokyo, Japan; [2]Toray Medical Co. Ltd, Tokyo, Japan*
*Critical Care* 2005, **9(Suppl 1):**P184 (DOI 10.1186/cc3247)

**Introduction** We previously reported that early introduction of hemoperfusion with an immobilized polymyxin B fiber column (PMX-DHP) improved life expectancy. This time, we report that early introduction of PMX-DHP eliminates humoral mediators and improves pulmonary oxygenation.
**Subjects and methods** Thirty-six sepsis patients were the subjects, consisting of 21 men and 15 women aged 62 ± 18.5 years. A thermodilution catheter was inserted in each patient, and the mixed venous oxygen saturation, oxygen delivery index, oxygen consumption index, and oxygen extraction ratio were measured. After it was confirmed that systemic oxygen metabolism was not impaired, PMX-DHP was started. Patients with uncontrolled infection were excluded from the study. The Acute Physiology and Chronic Health Evaluation (APACHE II) score was used as the index of severity, and survival of the patients was assessed after 1 month. The humoral mediators measured were IL-8 as a chemokine, plasminogen activator inhibitor-I (PAI-1) as an index of vascular endothelial cell activation, and polymorphonuclear neutrophil elastase (PMN-E) as an index of neutrophil activation. These mediators were measured before the start of PMX-DHP, and at 24, 48, and 78 hours after the start. The $PaO_2/FiO_2$ (P/F) ratio was used as an index of pulmonary oxygenation; it was measured before the start of PMX-DHP, and at 24, 48, 72, 92, and 120 hours after the start.
**Results** Due to the early introduction of PMX-DHP with oxygen metabolism as the index, all the patients remained alive after 1 month. Before the start, the APACHE II score was 24 ± 2.0. Before treatment, the IL-8 level was 54 ± 15.8 pg/ml, but it decreased significantly from 48 hours onwards. PAI-1 was 133 ± 28.1 before treatment, but decreased significantly from 48 hours onwards. Similarly, PMN-E was also a high 418 ± 72.1 before treatment, but improved significantly from 48 hours onwards. The P/F ratio was 228 ± 68 before treatment, but improved significantly from 96 hours onwards.
**Conclusion** The mechanism of action of PMX-DHP is still not fully understood, but the following findings were clarified from our investigation. (1) Early introduction of PMX-DHP improves life expectancy. (2) It is probable that changes of humoral mediators inhibit vascular endothelial cell activation, neutrophil activation, and chemokine activation. (3) It is probable that pulmonary oxygenation is improved due to elimination of humoral mediators.

**P185**

## Prehydration shifts the cytokine response towards a more anti-inflammatory balance during human endotoxemia

**P Pickkers, M Dorresteijn, L Van Eijk, M Netea, P Smits, H Van der Hoeven**
*University Hospital Nijmegen, The Netherlands*
*Critical Care* 2005, **9(Suppl 1):**P185 (DOI 10.1186/cc3248)

**Introduction** Animal experiments have shown that dehydration significantly alters the effects of endotoxin administration. Clinical

experience suggests that the administration of fluids in human endotoxemia causes an attenuation of symptoms. In the present study the effects of a standardised fluid protocol on symptoms, inflammatory and hemodynamic parameters in human endotoxemia are determined.

**Methods** With approval of the local ethics committee, 16 healthy volunteers received 2 ng/kg *Escherichia coli* endotoxin (O:113). After an overnight fast, seven subjects only received a continuous infusion of 75 ml/hour glc2.5%/NaCl 0.45% solution during the experiment ('non-prehydrated group'), while nine subjects received 1.5 l the hour prior to the endotoxin administration and 150 ml/hour during the course of the experiment ('prehydrated group'). In order to determine the inflammatory effects of the endotoxin CRP, white blood cell count and cytokine concentrations were determined at different time points. The course of body temperature was determined and subjects were asked to score the severity of their symptoms. Mean arterial pressure and heart rate were measured.

**Results** Prehydration reduced the inflammatory response after endotoxin administration. The induction of the proinflammatory cytokines (tumour necrosis factor alpha, IL-1β, IL-6, IL-8) was attenuated by the prehydration. The prehydrated group tumour necrosis factor alpha reached a peak value of 522 ± 63 pg/ml (mean ± standard error) compared with 927 ± 187 pg/ml in the non-prehydrated group (peak $P = 0.04$, analysis of variance [ANOVA] repeated measures $P = 0.046$). In contrast, the anti-inflammatory cytokine IL-10 demonstrated a trend towards higher values in the prehydrated group (prehydrated 117 ± 18 pg/ml and non-prehydrated 99 ± 18, $P$ = not significant). The prehydrated group developed a significantly lower fever (38.1 versus 38.8°C in the non-prehydrated group, $P < 0.05$), scored significantly lower on their symptom score (ANOVA repeated measures, $P = 0.036$) and recovered sooner. Endotoxin administration induced a 15 ± 3% and 15 ± 1% fall in MAP and an increase in heart rate (54 ± 2% and 47 ± 3%) in the prehydrated and non-prehydrated group, respectively. Both revealed no significant differences between groups.

**Conclusions** We demonstrate that prehydration significantly shifts the cytokine balance towards a more anti-inflammatory pattern in human endotoxemia. This effect is associated with a reduction in symptoms, whereas the changes in hemodynamic parameters are not influenced by prehydration. To correctly interpret the inflammatory effects of endotoxin in humans, the use of prehydration should be standardized.

## P186

### Repairing of acute lung injury by transvenous injection of bone marrow-derived stem cells

**K Sugahara, J Tokumine, K Teruya**
*University of the Ryukyus, Okinawa, Japan*
*Critical Care* 2005, **9(Suppl 1):**P186 (DOI 10.1186/cc3249)

**Introduction** Bone marrow stromal cells (BMSC) are progenitors for bone, cartilage, hematopoietic stroma, adipocyte, brain and neural cells. Recently some reports suggested that BMSC had a potency of differentiating lung epithelial cells. In this study, we tried to implant BMSC transvenously to a bleomycin-induced lung injury model, and evaluate the differentiation of BMSC.

**Materials and methods** The study was approved by the Institutional Review Boad. We used green fluorescent protein transgenic rats (green rat, TgN[act-EGFP] OsbCZ-004; Japan SLC Co.) as the BMSC donors, and SD rats as the bleomycin-induced lung injury model for BMSC recipients (Japan SLC Co.). Two days before BMSC implantation, bleomycin was injected transtracheally by transient tracheostomy in recipient SD rats. 5-FU (fluorouracil, antineoplastic agent) had been injected intraperitoneally into the green rats to increase the yield of BMSC. On the experiment day, the green rats were anesthetized, and then femurs were removed immediately, and a part of the bone cut to obtain BMSC. At the same time, the surgery of recipient SD rats was performed to identify and obtain the femoral veins, which were cannulated and filled with heparinized saline. The collected BMSC in a syringe were injected to recipient SD rats via the cannulated femoral vein for implantation. For the control sham operation, saline was injected instead of BMSC. Ten days, and 4 weeks after implantation, recipient rats were sacrificed and the lungs were fixed and examined.

**Results** We obtained well-proliferated BMSC. Then SMSC also had microspheres with good proliferation. We showed the presence of BMSC alive in the implanted lung tissue, and these BMSC spread widely. In a short survival, we did not find the alveolar cells expressing both SP-A and green fluorescent. In a long survival after implantation, we found that some small population of implanted BMSC expressed SP-A. The BMSC with histological SP-A-positive were present out of the vessels.

**Discussion** We showed excellent viability of BMSC and presence alive after transvenous implantation. We thought that the implanted BMSC remain in the vessel or migrate to the alveolus, and then some BMSC remaining in the vessel will migrate later and differentiate to the alveolar cells, which will contribute to constructing the injured lungs. Further studies are in progress to clarify differentiation of BMSC to alveolar cells.

**Acknowledgements** This study was supported in part by grants to KS and JT from the Japan Society for the Promotion of Science, and The Ministry of Education, Culture, Sports, Science and Technology, Japan.

## P187

### Cyclosporin A and a non-immunosuppressive derivative (NIM 811) improve survival and mitochondrial myocardial dysfunction in a murine model of severe sepsis by cecal ligation and puncture

**J Larché[1], S Lancel[2], A Gérard[1], R Nevière[2]**
*[1]CHU Brabois, Vandoeuvre-les-Nancy, France; [2]Lille 2 University, Lille, France*
*Critical Care* 2005, **9(Suppl 1):**P187 (DOI 10.1186/cc3250)

**Introduction** We have previously shown that apoptotic and myocardial mitochondrial respiratory abnormalities, occurring during severe sepsis in a murine model, can be prevented by overexpression of Bcl-2, a regulatory protein of mitochondrial function. So, we sought to evaluate, in this model, a pharmacological modulation by cyclosporin A (CsA), a mitochondrial permeability transition pore (MPTP) inhibitor, and by its non-immunosuppressive derivative *N*-methyl-4-isoleucin CsA (NIM 811).

**Materials and methods** Using a model of severe sepsis cecal ligation and puncture (CLP) induced (21-gauge needle) in female mice aged from 6 to 10 weeks, we studied the effects on 48-hour survival, echocardiographic data, myocardial apoptosis (nuclear apoptosis and caspase-3 and caspase-9 activation), and myocardial mitochondrial respiration, of MPTP inhibitors: CsA and NIM 811. A dose–response study was carried out with CsA in the following groups: CLP mice ($n = 15$), CLP + CsA 2 mg/kg ($n = 8$), CLP + CsA 10 mg/kg ($n = 20$), and CLP + CsA 100 mg/kg ($n = 5$). CsA was administered postoperatively, during the 1 ml subcutaneous injection for vascular filling. NIM 811 (dose of 2 mg/kg) was administered identically.

**Results** Compared with sham, CLP mice present a low 48-hour survival (32% vs 90%; $P < 0.05$), an increased shortening fraction at H24, and a greater myocardial apoptotic activity. Forty-eight-hour survival in septic mice is significantly improved with use of CsA or NIM 811 (100% vs 32%; $P < 0.05$). Low (2 mg/kg) or moderate (10 mg/kg) doses of CsA improve 48-hour survival. Shortening fraction increases early at H6 in the CLP + CsA group, and is normalized at H24. Myocardial nuclear apoptosis and caspase-3 and caspase-9 activation are prevented by CsA and NIM 811. We also observed, in the CLP group, an early increase of oxygen consumption, at the complex IV level of the mitochondrial respiratory chain. This was also prevented by MPTP inhibitors in the CLP + CsA and CLP + NIM 811 groups.
**Conclusion** These results suggest that mitochondrial respiration disruption could be responsible for myocardial dysfunction occurring during severe sepsis. To our knowledge, this is the first study addressing effects of NIM 811 in a severely septic animal model. Thus, the mitochondrial permeability transition pore constitutes a major target, and NIM 811 should be considered a therapeutic agent of potential great interest.

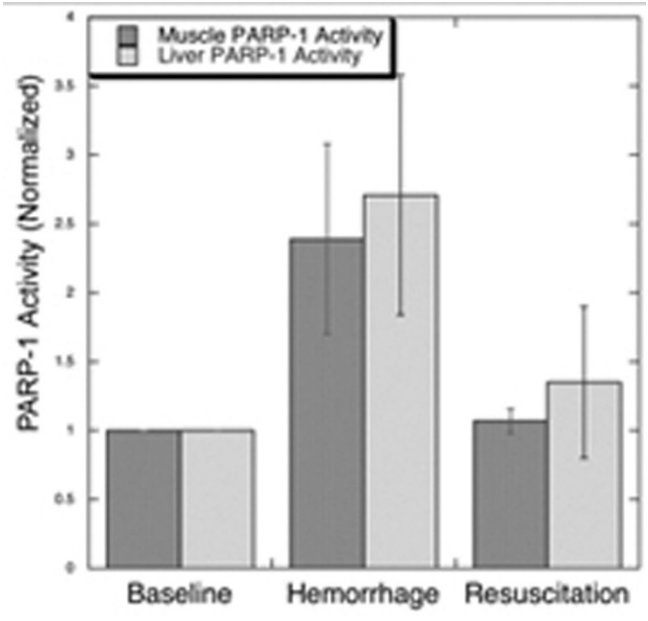
## P188

## Poly (ADP-ribose) polymerase activity during hemorrhagic shock and normotensive versus hypotensive resuscitation

**G Beilman[1], D Skarda[1], P Hergenrother[2], K Mulier[1]**
*[1]University of Minnesota, Minneapolis, MN, USA; [2]University of Illinois, Urbana, IL, USA*
*Critical Care* 2005, **9(Suppl 1):**P188 (DOI 10.1186/cc3251)

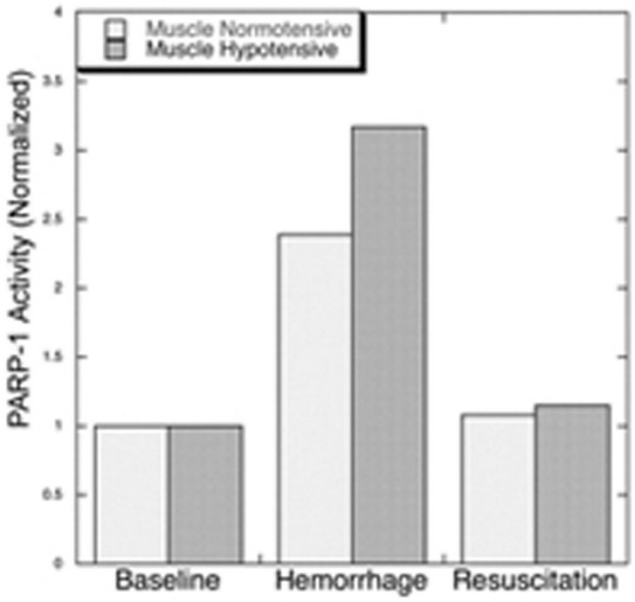
**Background** Poly (ADP-ribose) polymerase (PARP-1) over-activation may lead to depletion of NAD+ and ATP within the cell and proceed to necrotic cell death. Recently, published reports demonstrate high levels of PARP-1 activity in a model of porcine hemorrhagic shock. There is also increased interest in hypotensive resuscitation used for battlefield-wounded soldiers and trauma patients. We wished to evaluate PARP-1 activity during a model of porcine hemorrhagic shock with the hypothesis that PARP-1 activity will be increased using a hypotensive resuscitation strategy.
**Methods** Hemorrhagic shock was induced in splenectomized pigs with a 35% controlled hemorrhage via IVC cannula. Pigs were resuscitated to either normotensive (towards baseline) or hypotensive (80 mmHg) pressures using hextend and LR. Muscle and liver biopsies were taken prior to hemorrhage, after 90 min of shock, and after resuscitation. PARP-1 activity in biopsies was measured using chemical quantization of $NAD^+$. Physiologic and laboratory data collected during the experiment included blood pressure, heart rate, mean arterial pressure, cardiac output, oxygen delivery, oxygen consumption, and serum lactate.
**Results** Physiologic and laboratory parameters measured during the experiment were consistent with hemorrhagic shock, normotensive resuscitation and hypotensive resuscitation. PARP-1 activity increased from baseline with hemorrhage and returned towards baseline with resuscitation (Fig. 1). PARP-1 activity during normotensive resuscitation versus hypotensive resuscitation was not statistically different (Fig. 2).
**Conclusion** PARP-1 activity in our porcine model of hemorrhagic shock increases with the physiologic changes associated with shock. PARP-1 activity decreases with resuscitation in both normotensive and hypotensive resuscitation strategies. This provides evidence in support of short-term hypotensive resuscitation for hemorrhagic shock.

**Figure 1 (abstract P188)**




Poly (ADP-ribose) polymerase (PARP-1) activity increased with hemorrhage. With both normotensive and hypotensive resuscitation PARP activity returned towards baseline.

**Figure 2 (abstract P188)**




Muscle poly (ADP-ribose) polymerase (PARP-1) activity during normotensive resuscitation was not statistically different from that during hypotensive resuscitation.

**P189**

## Alpha-1-acid glycoprotein reduces hepatic leukocyte recruitment in early sepsis

**A Fox-Robichaud, H Kumar Ondiveeran, T McCurdy, W Sheffield**
*McMaster University, Hamilton, Canada*
*Critical Care* 2005, **9(Suppl 1):**P189 (DOI 10.1186/cc3252)

**Background** Alpha-1-acid glycoprotein (AGP) is a positive acute-phase circulating colloid reported to have anti-inflammatory properties. We have previously shown that hepatic leukocyte recruitment at 6 hours of sepsis varies with the choice of fluid used for resuscitation. Our objective in this study was to compare the ability of AGP versus normal saline (SAL) or albumin (ALB) to reduce the systemic inflammation associated with early sepsis.
**Methods** Human AGP and ALB were isolated and purified under pyrogen-free conditions from plasma. Sepsis was induced in male C57Bl/6 mice by cecal ligation and perforation (CLP) with an 18-gauge needle. Sham-operated (SHAM) and CLP mice received 2 ml subcutaneous saline before surgery. Mice received either 20 ml/kg SAL or 5 ml/kg of 3% AGP or 5% ALB in saline (matched for molar weight) as an intravenous bolus after inducing sepsis. The hepatic microcirculation was examined by intravital microscopy 4 hours later. Pulmonary inflammation was assessed by myeloperoxidase assay.
**Results** We have previously published that bolus SAL induces an increase in leukocyte rolling within the hepatic microcirculation. A similar finding was noted in the animals receiving saline in this study. Surprisingly, in the colloid-resuscitated CLP mice this rolling was reduced by 50%. In the central venules SHAM surgery did not induce significant leukocyte adhesion. CLP mice receiving SAL had a 30-fold increase in leukocyte adhesion, which was reduced by 30% when mice were treated with ALB and by 60% in those mice receiving AGP. Both colloids maintained sinusoidal perfusion during sepsis but there was a 20% reduction in perfusion in the SAL-treated CLP mice. Only treatment with AGP, however, was able to reduce the sepsis-induced increase in sinusoidal leukocyte adhesion to SHAM levels. At this early time point there was no evidence of neutrophil sequestration within the lungs as measured by myeloperoxidase assay.
**Conclusions** At 4 hours of sepsis there is evidence of hepatic but not pulmonary inflammation. In this model of early sepsis, treatment with a colloid significantly reduced the hepatic leukocyte–endothelial cell interactions compared with saline resuscitation. The presence of a glycosylated protein in the circulation appears to be more beneficial than albumin in limiting the systemic inflammatory response.

**P190**

## Protein C in murine neonatal sepsis

**E Muchitsch[1], H Schwarz[1], K Varadi[1], C Esmon[2], G Mancuso[3], G Teti[3]**
*[1]Baxter BioScience, Vienna, Austria; [2]Oklahoma Medical Research Foundation, Oklahoma City, OK, USA; [3]University of Messina, Italy*
*Critical Care* 2005, **9(Suppl 1):**P190 (DOI 10.1186/cc3253)

Neonatal sepsis is frequently associated with activation of the coagulation system. Generally, protein C levels are markedly reduced in the majority of septic patients, being associated with an increased risk of death. There is an activated protein C concentrate licensed for the treatment of severe sepsis in adults. However, the risk of severe bleeding may limit its use in neonates. Since the likelihood to induce bleeding with the zymogen form of protein C may be reduced, we therefore assessed both human and recombinant murine protein C zymogen in a murine neonatal sepsis model. In this model neonatal mice were challenged with viable group B streptococci (GBS). The impact of this septic condition on endogenous protein C levels was evaluated and the effect of treatment with either recombinant murine protein C or human plasma-derived (non-activated) protein C (Ceprotin®) investigated. During severe GBS sepsis murine endogenous protein C levels decreased over time in neonatal mice, resulting in a maximum decrease of 30% at 16 hours after GBS challenge and returned towards baseline at 30 hours. Concomitantly, there was an increase in endogenous protein C activation up to 59% at 6 hours after GBS challenge, returning to baseline levels at 16 hours. Blocking endogenous murine protein C with an anti-mouse monoclonal antibody increased the mortality rate significantly from 62% to 91%. Treatment of neonatal septic mice ($n = 36$) with 300 U/kg murine protein C subcutaneously 4 hours before GBS challenge decreases the mortality rate significantly in severe sepsis (LD90) to 64% ($P = 0.002$). Similarly, pretreatment with human plasma-derived protein C (200 U/kg) 4 hours before GBS challenge increased the survival rate significantly in severe septic mice. Human plasma derived protein C at the dose of 200 IU/kg was even effective given 18 hours after GBS challenge, leading to a decrease of the mortality rate in severe sepsis from 87.5% to 48%. Despite the species differences human protein C zymogen was activated to activated protein C and was detectable in the circulation of mice, showing a slow and low *in vivo* recovery, possibly due to the subcutaneous route of administration. This is the first preclinical study where a beneficial effect of a non-activated protein C could be shown in an animal model of severe neonatal sepsis.

**P191**

## The effect of activated protein C on experimental acute necrotizing pancreatitis

**L Yamanel[1], M Mas[1], B Comert[1], A Isik[1], S Aydin[2], N Mas[3], S Deveci[1], M Ozyurt[4], I Tasci[1], T Unal[1]**
*[1]GATA, Ankara, Turkey; [2]Numune Training and Research Hospital, Ankara, Turkey; [3]Hacettepe School of Medicine, Ankara, Turkey; [4]GATA, Istanbul, Turkey*
*Critical Care* 2005, **9(Suppl 1):**P191 (DOI 10.1186/cc3254)

**Introduction** Bacterial contamination has been estimated to occur in 30–40% of patients with necrotizing pancreatitis. Development of pancreatic necrosis mainly depends on the degree of inflammation and microvascular circulation of the pancreatic tissue. Translocation of bacteria from the gut is one of the most important factors in the development of septic complications and mortality in acute pancreatitis. We aimed to investigate the effect of activated protein C (APC) on histopathology and bacterial translocation in experimental acute necrotizing pancreatitis.
**Materials and methods** Forty-five male Sprague–Dawley rats were studied. Rats were randomly allocated into three groups. Acute pancreatitis was induced in Group II (positive control, $n = 15$), and Group III (treatment, $n = 15$) by retrograde injection of taurocholate into the common biliopancreatic duct. Group I rats (Sham, $n = 15$) received normal saline injection into the common biliopancreatic duct for mimicking the pressure effect. Group III rats were treated with intravenous activated protein C 6 hours after induction of pancreatitis. Pancreatic tissue samples were obtained from all animals for histopathological examination when they were sacrificed. Bacterial translocations to the pancreas, and mesenteric lymph nodes were examined.
**Results** Acute pancreatitis developed in all groups, but not in Group I (Sham), as indicated by microscopic parenchymal

necrosis, fat necrosis and abundant turbid peritoneal fluid. The pathologic score of the pancreatitis in the APC group ($10.31 \pm 0.47$) was lower when compared with the positive control group ($14.00 \pm 0.52$) ($P < 0.001$). Bacterial translocations to mesenteric lymph nodes and to the pancreas in the group treated with APC were significantly lower when compared with the control group ($P < 0.02$, and $P < 0.007$, respectively).

**Conclusion** We suggest that beneficial effect of APC on histopathology and bacterial translocation may be the results of improving pancreatic microcirculation and anti-inflammatory effect of APC.

## P192

### First experiences with protein C concentrate in adult patients with severe sepsis and septic shock associated to low protein C levels: a dose-finding study

**F Baratto[1], F Michielan[2], G Gagliardi[2], M Meroni[2]**
*[1]University of Padua, Padova, Italy; [2]University, Padua, Italy*
*Critical Care* 2005, **9(Suppl 1):**P192 (DOI 10.1186/cc3255)

**Aim** To describe the first experiences on the use of protein C concentrate (PC) in adult patients with severe sepsis and septic shock and clinical contraindications to activated protein C (APC). On the basis of the effectiveness demonstrated by the activated form in sepsis and of the encouraging results expressed in the literature of PC mainly about meningococcus fulminating infections, we carried out an observational study on PC with 28-day follow-up and a daily analysis of the hematochemical and clinical parameters. Particular attention was paid to the variations in the PC plasma levels, to the modifications of the coagulation system, to the SOFA score as well as to the safety under bleeding risk conditions. The study included 10 patients (seven females and three males) either with severe sepsis (four patients) or septic shock (six patients); one of them had DIC, with PC plasma levels less than 50%. APC could not be administered because of clinical reasons. Patients' mean age was 63.5 years (43–78), the average SAPS II was 51.8 (36–72), and the pathologies leading to sepsis were lung infections (three patients), peritonitis (five patients), and one patient with cutaneous and one patient with haematological origin. The average time elapsed between the onset of the organ failure and the beginning of treatment with PC was 27.7 hours (12–42).

**Results** Mortality on day 28 was 30% (three deaths), in all patients the PC plasma levels were brought again to the physiological values. The bolus-dose delivered was the following: UI of protein C = (100 – plasmatic basal level of PC) × body weight. It was followed by a continuos infusion of 3 IU/kg/hour for 72 hours. Among the parameters recorded during the PC infusion was observed in particular a significant decrease of PDFs, a general rise of the platelet count, and a reduction of the lactic acid levels. No adverse reaction or bleeding complication were seen, even if most of the patients' coagulation was altered or at risk due to neurological problems or repeated surgery.

**Conclusions** In our small number of patients, protein C concentrate has proven to be safe and particularly useful in the control of the coagulopathy triggered and sustained by sepsis.

**References**

1. Pescatore SL: **Clinical management of protein C deficiency.** *Expert Opin Pharmacother* 2001, **2:**431-439.
2. Fisher CJ Jr, Yan SB: **Protein C levels as a prognostic indicator of outcome in sepsis and related diseases.** *Crit Care Med* 2000, **28(9 suppl):**S49-S56.
3. Clarke RCN, Johnston JR, Mayne EE: **Meningococcal septicaemia: treatment with protein C concentrate.** *Intensive Care Med* 2000, **26:**471-473.
4. De Kleijn ED, De Groot R, Hack CE, H Mulder PG, Engl W, Moritz B, Joosten KF, Hazelzet JA: **Activation of protein C following infusion of protein C concentrate in children with severe meningococcal sepsis and purpura fulminans: a randomized, double-blinded, placebo-controlled, dose-finding study.** *Crit Care Med* 2003, **31:**1839-1847.
5. Fourrier F, Leclerc F, Aidan K, Sadik A, Jourdan M, Tournois A, *et al.*: **Combined antithrombin and protein C supplementation in meningococceal purpura fulminans: a pharmacokinetic study.** *Intensive Care Med* 2003, **28:**1081-1087.
6. Makris PE, Girtovitis F, Papadopulos A, Tamioulaki A, Kosmidou M, Pithara E: **Treatment of DIC the role of PC.** *J Thromb Haemost* 2003, **1:**P0600.
7. Schellongowski P, Bauer E, Locker G, Frass M, Staudinger T, Knobl P: **Treatment of adults with sepsis-induced coagulopathy and purpura fulminans with a plasma-derived protein C concentrate (Ceprotin).** *Crit Care Med* 2003, **(suppl 2):**P021.

## P193

### Eligibility for drotrecogin alfa therapy on the basis of APACHE II score and organ failure

**R Shulman[1], S Bagga[2]**
*[1]University College London Hospitals, London, UK; [2]School of Pharmacy, London, UK*
*Critical Care* 2005, **9(Suppl 1):**P193 (DOI 10.1186/cc3256)

**Introduction** Drotrecogin alfa was licensed for severe sepsis in Europe in patients with >1 organ failure (OF); in contrast to the USA where it is licensed on the basis of APACHE II score > 24. At our institution, the drug and therapeutics committee (despite ICU representation) insisted that the drug should be reserved for patients with an APACHE II score > 24 and >1 OF. Following 1 year of use, there was a concern that only one patient received the drug. To investigate the reason for this, we conducted this study to establish what proportion of patients fitted our criteria and whether suitable patients were missed.

**Aims** To assess patients with APACHE II score > 24 for their suitability for drotrecogin alfa therapy. To establish whether patients met the inclusion criteria and exclusion criteria. Additionally, to follow the outcome of those who were suitable for the drug.

**Method** Using the GE Medical Systems QS Clinical Information System, the last 50 patients with APACHE II score > 24 were identified from 23 March 2004 to 1 June 2004 (70 days). They were retrospectively assessed to identify whether they met the organ failure criteria from the Prowess study [1] and the SIRS criteria [1]. Patients were deemed unsuitable if they did not have a realistic chance of recovery on admission. This was reviewed by the ICU pharmacist and clinical director. Infection was regarded as those being treated with an antibiotic within the first 48 hours (microbiologists advised on all antibiotic prescribing).

**Results** During the monitoring period, 222 ICU patients were admitted. Of the 50 patients with APACHE II score > 24, 46% met the SIRS criteria, 54% had >1 OF and 58% had signs of an infection. Seventy per cent of patients had contraindications to drotrecogin alfa use, the most common being active internal bleeding, recent major surgery and GI bleeding within 6 weeks (12% each). Only one patient (0.45% of admissions) met all the suitability criteria. This same patient was the only case where the drug was used; the patient initially rallied but died 7 days later.

**Conclusion** The single patient who fitted the criteria received the drug, but did not survive. For severely septic patients, using the criteria of APACHE II score > 24 and >1 OF for suitability of treatment with drotrecogin alfa resulted in an extremely low proportion of patients who were eligible for therapy. These criteria should be reviewed so a wider population may benefit from this drug.

**Reference**

1. Bernard G, *et al.*: *N Engl J Med* 2001, **344:**699-709.

## P194

### Canadian ENHANCE data support the efficacy and safety of drotrecogin alfa (activated) despite higher disease severity than the global ENHANCE population

**R Hall[1], H Fisher[2], J Marshall[3], R Hodder[4], J Russell[5], B Lee[2]**
*[1]Queen Elizabeth II HSC, Halifax, Canada; [2]Eli Lilly Canada Inc., Toronto, Canada; [3]University of Toronto, ON, Canada; [4]University of Ottawa, Canada; [5]St Paul's Hospital, Vancouver, BC, Canada*
*Critical Care* 2005, **9(Suppl 1):**P194 (DOI 10.1186/cc3257)

The ENHANCE trial was an open-label, multi-national (25 countries) study of drotrecogin alfa (activated) (DrotAA) in 2378 patients with severe sepsis (systemic inflammatory response due to acute infection and ≥ 1 sepsis-induced organ dysfunction of ≤ 48 hours duration). In Canada, 305 patients were enrolled at 18 sites. DrotAA was infused for 96 hours at 24 mg/kg/hour. Patients continued to receive supportive care. Table 1 presents baseline characteristics, bleeding events, and 28-day all-cause mortality for Canadian and Global ENHANCE populations. Canadian patients demonstrated higher disease severity at baseline by organ dysfunction and APACHE II, yet had numerically lower mortality and fewer infusion period serious bleeds than the Global ENHANCE overall population. Comparison of laboratory and severity variables between survivors and non-survivors using the Wilcoxon two-sample test suggests that possible predictors of survival in Canadian ENHANCE patients were: first day change in creatinine; number of organ failures at baseline; pre-infusion APACHE II score; and enrollment at PROWESS study sites. In conclusion, differences were observed in disease severity and outcomes in Canadian ENHANCE patients compared with the overall trial sample.

**Table 1**

| Baseline characteristics and outcomes | Canadian ENHANCE ($n = 305$) | Global ENHANCE ($n = 2378$) |
|---|---|---|
| Mean age, years (SD) | 56.9 (17.2) | 59.1 (16.9) |
| APACHE II ICU (SD) | 25.3 (7.8) | 22.0 (7.4) |
| # Organ failure (SD) | 3.1 (1.2) | 2.7 (1.1) |
| Baseline SOFA (SD) | 10.9 (3.6) | 9.7 (3.5) |
| Vasopressor use (%) | 82% | 74% |
| Mechanical ventilation (%) | 90% | 82% |
| Infusion serious bleed (%) | 2.0% | 3.6% |
| 28-Day serious bleed (%) | 3.9% | 6.5% |
| Infusion ICH (%) | 0.3% | 0.6% |
| 28-Day mortality (%) | 22.6% | 25.3% |

SD, standard deviation.

## P195

### Activated protein C in sepsis: an Indian experience

**B Abraham, M Mohan, J Raja, N Ramakrishnan**
*Apollo Hospitals, Chennai, India*
*Critical Care* 2005, **9(Suppl 1):**P195 (DOI 10.1186/cc3258)

**Background** The PROWESS study has shown that the use of recombinant human activated protein C (rhAPC) can reduce mortality in severe sepsis [1]. The effect of this novel drug in a Third World setting has never been explored. The aim of this study is to see whether all the end points of the PROWESS study could be reproduced in the Indian population.

**Method** A prospective, single-center observational study. Consecutive patients who fulfilled the inclusion criteria of the PROWESS study [1] were included into the study. The study group was patients who received rhAPC. Patients who did not receive rhAPC formed the control group. Data collected were demographics, details of premorbid conditions and organ function, markers of disease severity and infection. APACHE II scores were recorded at baseline. Organ dysfunction was measured using SOFA scoring. The primary end point was all-cause mortality at 28 days. Secondary end points were morbidity as measured by SOFA scores and the incidence of adverse events. Data are expressed as mean ± standard deviation. The results were analysed using Fisher's exact test and unpaired *t* tests. $P < 0.05$ was considered significant.

**Results** A total of 25 patients were enrolled into the study (study group – 14 and controls – 11). Both groups were similar in terms of age and sex distribution, demographics, comorbidities, baseline APACHE II score, ventilatory and inotropic support and number of organ dysfunction. In the study group only 27% had an APACHE II score > 25. Treatment with rhAPC was started at a mean of 34.9 ± 21.9 hours from the onset of first organ dysfunction or admission, whichever occurred earlier. The 28-day mortality in our study was 36% in the study group as compared with 64% in the controls. This was not statistically significant. There was an improvement in the SOFA score on day 7 in 57% of the study group and 36% of controls. The only adverse event noted was bleeding. Minor bleeding was seen in 64% of the study group, which was significantly higher than that in 18% of controls.

**Conclusion** This study is not powered to come to any definitive conclusion. There was a trend towards decreasing mortality in patients treated with rhAPC as compared with the controls and there was also a decrease in morbidity in the study group as assessed by the SOFA scores. The incidence of bleeding, even though minor, was significantly higher in the study group. However, unlike in the PROWESS study, only 27% of the study group had an APACHE II score > 25 despite 43% of them having three or more organ system failures. This brings up the question of whether the APACHE II score can be used as a marker of severity of illness in the Indian population? The high cost of the drug is a concern in the Indian setting where most patients rely on their own resources for funding such drugs. The only way these questions can be answered is by having a well-designed and powered study conducted in the Indian population.

**Reference**

1. Bernard GR, Vincent JL, Laterre PF, *et al.*: **Efficacy and safety of recombinant human activated protein C for severe sepsis.** *N Engl J Med* 2001, **344:**699-709.

## P196

### Epidemiology of severe sepsis and septic shock in Germany: results from the German 'Prevalence' study

**FM Brunkhorst, C Engel, K Reinhart, H-G Bone, R Brunkhorst, H Burchardi, K-U Eckhardt, H Forst, H Gerlach, S Grond, M Gründling, G Huhle, M Oppert, D Olthoff, M Quintel, M Ragaller, R Rossaint, W Seeger, F Stüber, N Weiler, T Welte, M Loeffler, for the German Competence Network Sepsis**
*SepNet Office, Department of Anaesthesiology and Intensive Care Medicine, Friedrich-Schiller-University Jena, Germany*
*Critical Care* 2005, **9(Suppl 1):**P196 (DOI 10.1186/cc3259)

Although a large number of epidemiological sepsis studies have been performed in Europe and the United States in the past years, sound data for Germany are so far lacking. In the 'Prevalence of Severe Sepsis and Septic Shock in Intensive Care Units in

Germany' study, a prospective observational cross-sectional study, the network gathered data from 454 randomly selected ICUs in 310 hospitals in Germany and screened 3877 patients – according to the ACCP/SCCM Consensus Conference criteria – by local 1-day visits of trained physicians from the 17 German Competence Network Sepsis (SepNet) regional study centers. Visits were randomly distributed over a 1-year period (2003) to allow assessment of seasonal variations of sepsis prevalence. The ICU sample was taken from a registry of all German hospitals with ICUs (1380 hospitals with 2075 ICUs). Pediatric ICUs were not considered. The study was completed in January 2004 and the database was closed on 31 May. Seven percent of ICUs were situated in university, 34% in university-affiliated and 53% in general hospitals. Fifty-six percent of ICU directors were anesthesiologists and 26% internists. An infection was microbiologically documented in 22% and diagnosed by clinical criteria alone in 12% of screened patients. Respiratory tract infections were most common (52%), followed by intra-abdominal (15%) and urogenital infections (7%). Gram-negative and Gram-positive infections were nearly equally distributed (33% vs 35%); in 16% a fungal infection was suspected. The prevalence of sepsis was 12%, infection without SIRS was 7%, and severe sepsis/septic shock was 11%. There were significant differences in the prevalence of severe sepsis/septic shock over 1 year with the highest prevalence in May/June 2003 (18%). The infection was ICU acquired in 37%, hospital acquired in 20% and community acquired in 35.5%. ICU mortality in patients with severe sepsis/septic shock was 47% and hospital mortality was 54%. Based on these findings the incidence of severe sepsis/septic shock in German ICUs can be estimated as 75,000 cases per year (110 per 100,000 inhabitants), comparable with the incidence of acute myocardial infarction (143 per 100,000 inhabitants). With an estimated 40,000 deaths per year, severe sepsis/septic shock is the third most frequent cause of death in Germany after coronary artery disease and acute myocardial infarction.

Incidence and mortality rate of severe sepsis and septic shock in German ICUs are higher than reported in recent studies. This may be due to the representative sample size, the more standardized diagnostic criteria and a lower interobserver variability.

**Acknowledgements** Supported by the German Federal Ministry of Education and Research (BMBF), Grant No: 01 KI 0106 and Lilly Deutschland GmbH.

## P197

## Sepsis Brazil: an epidemiological study in intensive care units

**J Sales[1], C David[1], P Souza[2], M Knibel[3], R Hatum[3], F Dias[4], A Neto[5], C Pinheiro[6], S Lima[7], A Japiassú[8], S Lobo[9], A Estrada[10], J Anjos[11], Sepsis Study Group[12]**

*[1]HUCFF-UFRJ, Rio de Janeiro, Brazil; [2]Hospital Clínicas Niterói, Brazil; [3]H São Lucas, Rio de Janeiro, Brazil; [4]H São Lucas, Porto Alegre, Brazil; [5]H do Trabalhador, Curitiba, Brazil; [6]H Clínicas, Porto Alegre, Brazil; [7]H VOT Penitência, Rio de Janeiro, Brazil; [8]H Quinta Dor, Rio de Janeiro, Brazil; [9]H de Base, S J Rio Preto, Brazil; [10]H Doenças Tropicais, Goiânia, Brazil; [11]H Madre Tereza, Belo Horizonte, Brazil; [12]Fundo AMIB, São Paulo, Brazil*

*Critical Care* 2005, **9(Suppl 1):**P197 (DOI 10.1186/cc3260)

**Introduction** Sepsis represents the major cause of death in the ICUs all over the world. Many studies have shown an increasing incidence over time and only a slight reduce in mortality. Many new treatment strategies are arising and we should know our incidence of sepsis and features.

**Methods** A prospective cohort study in 50 hospitals of all regions of Brazil. The patients who were admitted or who developed sepsis during the month of September 2003 were enrolled. They were followed until the 28th day. The diagnoses were made in accordance with the criteria proposed by ACCP/SCCM. Demographic features, APACHE II score, Sepsis-related Organ Failure Assessment (SOFA) score, mortality, sources of infections and lengh of stay (LOS) were evaluated.

**Results** A total of 2419 patients were identified and 409 (16.9%) filled the criteria of sepsis, severe sepsis or septic shock. The average age was 61.9 years, 225 (55%) were male, and the overall 28-day mortality rate was 46.2%. The average APACHE II score was 21 and the SOFA score on the first day was 7. The SOFA score in the mortality group was higher on day 1 (8), and had increased on day 3. We observed 326 episodes of sepsis, 118 (28.9%) patients with severe sepsis, and 210 (51.4%) patients with septic shock. The mortality rate for sepsis, severe sepsis and septic shock was 15%, 35.6% and 63.8%, respectively. The average LOS was 16 days. The main source of infection was the respiratory tract (71.6%). Gram-negative bacilli were more prevalent (55.6%). Gram-positive cocci accounted for 32% and fungi infections for 10.6%.

**Conclusion** A high incidence and mortality of sepsis in ICUs in our country was observed. The high frequency of severe sepsis and septic shock demonstrated a group at high risk of death. In order to have a better use of the resources and to promote a reduction in mortality in the next 5 years it is very important to identify our specific features. After the final analysis of the database we intend to give our contribution to a better understanding of sepsis in Brazil.

## P198

## Costs of severe sepsis according to the guidelines of the 'Surviving Sepsis Campaign'

**G Vazquez de Anda, T Mondragon Rangel, J Arzate Villafaña, A Mondragon, A Jimenez, M Gomez**

*ISSEMYM Medical Center, Toluca, Mexico*

*Critical Care* 2005, **9(Suppl 1):**P198 (DOI 10.1186/cc3261)

**Introduction** Despite advanced organ support, patients suffering from severe sepsis still have a high mortality rate [1]. Recently, it has been advocated to follow the 'Surviving Sepsis Campaign' (SSC) [2] to treat patients suffering from severe sepsis. Even though it is unpredictable which patient will survive and for what reason, an important amount of the ICU budget has to be invested on drugs and supplies (DS). Therefore, the present study aimed to determine the amount of money that our ICU (which is administrated by public funds) has to invest on DS to treat a patient suffering from severe sepsis.

**Methods** Data on costs for DS were recorded daily for every patient admitted to the ICU from June to October 2004. Patients with severe sepsis were separated from the main database. Costs for each item of the SSC (including activated protein C) were taken as independent variables, and the survey as a dependent variable. We used the cost of each DS exactly as it was sold to our institution. Costs are presented in Euros according to the currency rate at 30 October 2004.

**Results** During the 5-month period, 211 patients were admitted to the ICU. The treatment for severe sepsis according to the SSC was affordable for all patients admitted to the ICU. The cost for DS during this period was €327,026.36. Of all ICU patients, 37 (17.53%) suffered from severe sepsis and the DS cost for this group was €146,513.10. Postoperative sepsis was observed in 18 patients (48.6%) while 19 (51.3%) were non-postoperative sepsis; the cost for DS in these two groups was €58,294.61 and €88,218.49, respectively. The total costs for DS to produce a

43% survival on severe sepsis was €55,121.38; that is, postoperative sepsis €30,253.91 and non-postoperative sepsis €24,867.48. The cost for patients who died was €91,391.72. Patients who died with non-postoperative sepsis had the highest DS costs (i.e. €63,351.01). The investment to save 16 patients was €63,357.02.

**Conclusions** In our ICU, and following the SSC guidelines, we have to invest in every patient suffering from severe sepsis at least €9157.07 to produce a 43% survival. That means, in the future, any increase in survival with the same investment on DS may reflect our best approach to treat severe sepsis.

**References**

1. Moerer O, Burchardi H: **The costs of sepsis.** *ICU management* 2004, **4:**25-29.
2. Dellinger PR, Carlet JM, Masur H, Gerlach H, Calandra T, *et al.*: **Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock.** *Crit Care Med* 2004, **32:**858-873.

## P199

### Selective poly(ADP-ribose)-polymerase inhibition affects neither DNA repair nor cell senescence after ischemia-reperfusion

**B Hauser[1], U Ehrmann[2], M Albicini[2], M Gröger[2], P Radermacher[2], C Szabó[3], J Kick[2]**
*[1]Semmelweis University, Budapest, Hungary; [2]University of Ulm, Germany; [3]Inotek Pharmaceuticals, Beverly, MA, USA*
*Critical Care* 2005, **9(Suppl 1):**P199 (DOI 10.1186/cc3262)

**Background** Poly(ADP-ribose)-polymerase (PARP) inhibition has been beneficial in different models (sepsis, ischemia-reperfusion [I/R], hemorrhage) where oxidative stress induced DNA damage and subsequent PARP activation plays an important role. The effect of PARP inhibition on DNA repair in this context, however, is unknown. We therefore tested the effect of the selective PARP-1 blocker INO-1001 on DNA repair and cell senescence in a porcine model of thoracic aortic cross-clamping.

**Materials and methods** After instrumentation, anesthetized and mechanically ventilated pigs received vehicle ($n = 9$) or INO-1001 ($n = 9$, 2 mg/kg each before clamping and during reperfusion, respectively). Norepinephrine (NE) was infused after declamping as required to maintain mean arterial pressure $\geq 80\%$ of the preclamping level. Hemodynamic and metabolic data were recorded before clamping as well as prior to and 2 and 4 hours after declamping. The effect of INO-1001 on DNA damage and repair (single-cell gel electrophoresis, 'comet assay') was evaluated *ex vivo* in isolated lymphocytes (Ficoll gradient) that were sampled immediately before clamping, subsequently exposed to 4 bar of 100% $O_2$ in a hyperbaric chamber (HBO) for 2 hours and analyzed before as well as immediately 1 and 2 hours after HBO. Surgery and I/R-related DNA damage *in vivo* was assessed in whole blood samples taken before surgery, before clamping, and before and 2 hours after declamping. At the end of the experiment the spinal cord, gut, liver, and kidney tissue specimens were sampled for immonuhistochemistry of cyclin-dependent kinase inhibitor (p21 and p27) gene expression as a measure of cell senescence. Data are median (minimum–maximum).

**Results** Significantly shorter NE infusion time (53 [23–93] vs 70 [41–83] min, $P = 0.042$) with reduced total NE doses (12 [6–19] vs 22 [9–38] μg/kg, $P = 0.034$) were needed for hemodynamic management in the INO-1001-treated animals. The time course of both the HBO-induced and surgery and I/R-related oxidative DNA damage was identical in the two groups. There were no differences in p21 and p27 expression, either.

**Conclusion** The markedly reduced NE infusion time and dose needed for post-I/R hemodynamic stabilization confirm the well-known positive inotropic effect of selective PARP-1 blockers [1]. INO-1001 proved to be safe with respect to DNA repair and cell senescence.

**Acknowledgements** Supported by the Alexander-von-Humboldt-Stiftung (BH) and Land Baden-Württemberg, Germany (MG).

**Reference**

1. Szabó G, *et al.*: *S*hock 2004, **21:**426-432.

## P200

### Rosiglitazone, a peroxisome proliferator-activated receptor-gamma agonist, attenuates intercellular adhesion molecule-1 and cytokine-induced neutrophil chemoattractant-1 expression in lungs of rats with acute lung injury

**D Liu[1], B Zeng[1], S Zhang[1,2], Z Geng[2]**
*[1]Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, WuHan, China; [2]Lanzhou General Hospital, Lanzhou Command of PLA, LanZhou, China*
*Critical Care* 2005, **9(Suppl 1):**P200 (DOI 10.1186/cc3263)

**Aim** To investigate the effects of rosiglitazone (ROSI), a peroxisome proliferator-activated receptor-gamma (PPAR-γ) agonist, on the lung expression of intercellular adhesion molecule-1 (ICAM-1) and cytokine-induced neutrophil chemoattractant-1 (CINC-1) in rats with acute lung injury.

**Methods** Thirty-six anesthetized male Wistar rats were randomly divided into six groups: DMSO control group, ROSI group, GW9662 group, lipopolysaccharide (LPS) group, ROSI + LPS group and GW9662 + ROSI group. Rats received either LPS (6 mg/kg intravenously) or vehicle (saline, 2 ml/kg intravenously). ROSI (0.3 mg/kg intravenously) or vehicle (10% DMSO) was administered 30 min before treatment with LPS. The selective PPAR-γ antagonist, GW9662 (0.3 mg/kg intravenously), was given 20 min before ROSI. Four hours after LPS injection, the wet/dry lung weight (W/D) ratio, myeloperoxidase (MPO) activity, malondialdehyde (MDA) and CINC-1 concentrations were assayed in the lung tissues. Immunohistochemical analysis of ICAM-1 expression was also studied.

**Results** Pretreatment with ROSI attenuated LPS-induced increases of the W/D ratio, MPO activity, MDA and CINC-1 concentrations as well as the expression of ICAM-1 in the lung tissues ($P < 0.01$). The specific PPAR-γ antagonist GW9662 significantly antagonized the effects of ROSI.

**Conclusion** Pretreatment with ROSI significantly reduces endotoxin-induced acute lung injury in rats; the mechanism may be through activation of PPAR-γ accompanied by inhibition of ICAM-1 and CINC-1 expression.

## P201

### Protective effects of rosiglitazone, a peroxisome proliferator-activated receptor-gamma agonist, on endotoxin-induced acute lung injury in rats

**D Liu[1], B Zeng[1], S Zhang[1], Y Wang[1], L Zeng[1], Z Geng[2]**
*[1]Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, WuHan, China; [2]Lanzhou General Hospital, Lanzhou Command of PLA, LanZhou, China*
*Critical Care* 2005, **9(Suppl 1):**P201 (DOI 10.1186/cc3264)

**Objective** To determine whether rosiglitazone, a peroxisome proliferator-activated receptor-gamma (PPAR-γ) agonist, decreases the severity of endotoxin-induced acute lung injury and to investigate cellular mechanisms contributing to these effects.

**Setting** A university research laboratory.

**Interventions** Male Wistar rats were allocated into six groups ($n = 6$ for each group): (a) Sham-vehicle group: rats were treated with 10% dimethyl sulphoxide (DMSO) (vehicle for rosiglitazone) 30 min prior to saline; (b) Sham-rosiglitazone group: same as the Sham-vehicle group except that rosiglitazone (0.3 mg/kg, intravenously [i.v.]) was administered instead of DMSO; (c) Sham-GW9662 group: identical to Sham-vehicle group except that GW9662 (0.3 mg/kg, i.v.) was administered instead of DMSO; (d) LPS-vehicle group: rats were treated with DMSO 30 min before they were challenged with lipopolysaccharide (LPS) (6 mg/kg, i.v.); (e) Rosiglitazone-LPS group: rats were treated with rosiglitazone 30 min before they were subjected to LPS; (f) GW9662-rosiglitazone group: identical to Rosiglitazone-LPS group, but GW9662 was administered 20 min before rosiglitazone. Rats were killed at 4 hours after the injection of LPS and the lungs were collected.
**Measurements and results:** Pretreatment with rosiglitazone markedly attenuated the degree of (a) tissue injury and pulmonary edema, (b) neutrophils infiltration and lipid peroxidation, (c) expression of inducible nitric oxide synthase and production of nitric oxide, (d) formation of nitrotyrosine in the lungs of LPS-treated rats. The specific PPAR-γ antagonist GW9662 significantly antagonized the effects of rosiglitazone.
**Conclusions** These findings support the view that rosiglitazone and other potent PPAR-γ agonists may be useful in the therapy of endotoxin-induced acute lung injury.

## P202

## Epithelial lining fluid analysis

**A Ishizaka**
*Keio University Hospital, Tokyo, Japan*
*Critical Care* 2005, **9(Suppl 1):**P202 (DOI 10.1186/cc3265)

A noninvasive bronchoscopic microsampling (BMS) probe was developed to sample biochemical constituents of the epithelial lining fluid in small airways. In this method, intratracheal saline instillation is not required. Therefore, hypoxemia after BAL and dissemination of airway infection can be avoided. We performed the following two studies in acute respiratory distress syndrome (ARDS) patients.
(1) BMS was applied in a control group of seven patients who had hemoptysis or small solitary peripheral nodules but no hypoxemia or other signs of acute inflammation and in four patients with ARDS, to test whether BMS can ascertain the presence of acute pulmonary inflammation without complications. Complications, including a significant decrease in arterial oxygen saturation, were observed neither during nor after BMS. In the ARDS, albumin, lactate dehydrogenase (LDH), IL-6, basic fibroblast growth factor, and neutrophil elastase concentrations in epithelial lining fluid were significantly higher ($P < 0.0001$, $P = 0.012$, $P < 0.0001$, $P < 0.0001$, and $P < 0.0001$, respectively) than in the control group.
(2) KL-6 is a pulmonary epithelial mucin more prominently expressed on the surface membrane of alveolar type II cells when these cells are proliferating, stimulated, and/or injured. We hypothesized that high levels of KL-6 in epithelial lining fluid and plasma would reflect the severity of lung injury in patients with acute lung injury (ALI). Epithelial lining fluid was obtained at onset (day 0) and day 1 of ARDS/ALI by BMS in 35 patients. On day 0, KL-6 and albumin concentrations in epithelial lining fluid were significantly higher than in normal controls ($P < 0.001$), and the concentrations of KL-6 in epithelial lining fluid ($P < 0.002$) and in plasma ($P < 0.0001$) were higher in nonsurvivors than in survivors of ALI/ARDS. These observations were corroborated by the immunohistochemical localization of KL-6 protein expression in the lungs of nonsurvivors with ALI and KL-6 secretion from cultured human alveolar type II cells stimulated by proinflammatory cytokines. Because injury to distal lung epithelial cells, including alveolar type II cells, is important in the pathogenesis of ALI, the elevation of KL-6 concentrations in plasma and epithelial lining fluid could be valuable indicators for poor prognosis in clinical ALI.
We are now performing proteomic analysis of ELF obtained from ARDS to find key proteins for its pathogenesis.

## P203

## Ketoconazole for the prevention of ARDS: review of the literature and novel hypothesis

**W Haddara**
*London Health Sciences Center, London, Canada*
*Critical Care* 2005, **9(Suppl 1):**P203 (DOI 10.1186/cc3266)

**Introduction** Ketoconazole has been shown in several clinical trials to reduce the risk of developing ARDS in populations at risk. Despite the clinical trials, its use remains limited.
**Methods** Literature review and synthesis.
**Results** Two small randomized controlled trials found that Ketoconazole prevents the development of ARDS in mixed and septic surgical ICU populations [1,2]. A third study examined the effect of a guideline implementation for the use of Ketoconazole to prevent ARDS and found that postguideline implementation rates of ARDS were significantly lower than both historical rates and rates in another hospital that did not implement the guideline [3]. A historical case control study of Ketoconazole for prevention of ARDS post-esophagectomy also found a significant reduction [4]. The ARDSNet trial examined the use of Ketoconazole in a prospective design and found no difference in ARDS rates [5]. However, the majority (77%) of patients enrolled in the trial had established ARDS (defined by $PaO_2/FiO_2$ ratio < 200). Ketoconazole has been shown to reduce a number of mediators involved in the development of acute lung injury and may therefore prevent ARDS if given prior to the onset of severe ALI. The mechanism may involve modulation of the cytochrome p450 enzyme system. Various cytochrome p450 isozymes have been shown to be involved in the inflammatory response that underlies acute lung injury.
**Discussion** The ARDSNet trial has had a negative impact on the use of Ketoconazole for prevention of ARDS despite the stated objective of the trial to examine the role of Ketoconazole in treatment of early ARDS rather than prevention of ARDS. The use of Ketoconazole has been further hampered by the lack of a plausible biological mechanism.
**Conclusions** An adequately powered randomized controlled trial is needed to assess the role of Ketoconazole in preventing ARDS.
**References**
1. Slotman GJ, *et al.*: *J Trauma* 1988, **28:**648-654.
2. Yu M, Tomasa G: *Crit Care Med* 1993, **21:**1635-1642.
3. Sinuff T, *et al.*: *J Crit Care* 1999, **14:**1-6.
4. Schilling MK, *et al.*: *Dis Esophagus* 2001, **14:**37-40.
5. The ARDS Network. *JAMA* 2000, **283:**1995-2002.

## P204

## Endothelial nitric oxide synthase is a regulator of hemodynamics in sepsis

**M Merx[1], J Graf[1], A Goedecke[2], M Goldnau[1], J Kellinghaus[1], U Janssens[1], R Luetticken[1], P Hanrath[1], C Weber[1], J Schrader[2]**
*[1]Universitaetsklinikum, RWTH Aachen, Germany; [2]Heinrich Heine Universitaet, Duesseldorf, Germany*
*Critical Care* 2005, **9(Suppl 1):**P204 (DOI 10.1186/cc3267)

**Background** While inducible nitric oxide synthase (iNOS) is believed to be the high-capacity NO-producing enzyme

responsible for the detrimental hemodynamic alterations observed during sepsis, the role of endothelial nitric oxide synthase (eNOS) remains more obscure. Thus, it was the present study's aim to elucidate the influence of eNOS on hemodynamics in septic shock using $eNOS^{-/-}$ mice in the clinically relevant polimicrobial cecum ligation and puncture (CLP) model of sepsis.

**Methods and results** Prolonged survival was observed in $eNOS^{-/-}$ mice (68 ± 25 hours vs 25 ± 6 hours in WT mice, $n = 12$, $P < 0.001$). Chronic unselective NOS inhibition with ethylthiourea (ETU) in $eNOS^{-/-}$ mice after sepsis induction diminished this survival benefit, while ETU application in WT mice after CLP led to slight improvement in survival time. Cardiac output, studied by serial echocardiography, increased to a maximum of 60% over baseline at 10 hours after sepsis induction in WT mice but not in septic $eNOS^{-/-}$ mice and septic mice (WT and $eNOS^{-/-}$) treated by unselective NOS inhibition. WT CLP mice were refractory to β-stimulation, while $eNOS^{-/-}$ CLP mice responded comparably with sham-operated WT mice. Mean arterial blood pressure was decreased by 25 ± 8 mmHg ($P < 0.001$; $n = 8$) in WT CLP mice, with $eNOS^{-/-}$ CLP mice showing no sign of hypotension. Contractility of isolated WT CLP hearts was impaired by 35% ($P < 0.001$, $n = 8$), but hearts from CLP $eNOS^{-/-}$ mice remained unaltered. While eNOS expression remained stable, coronary flow studies indicated a high level of eNOS activation secondary to sepsis.

**Conclusion** eNOS is a key player in the hemodynamics of sepsis. Selective eNOS inhibition appears beneficial in this model of sepsis with global nitric oxide synthase inhibition diminishing most of the observed benefit.

## P205

### Application of the bovine hemoglobin solution HBOC-301 with and without isovolemic hemodilution reduces the histopathologic damage in acute severe pancreatitis in swine

**M Freitag, O Mann, T Strate, A Gottschalk, S Petri, C Rempf, J Izbicki, T Standl**

*University Hospital Hamburg-Eppendorf (UKE), Hamburg, Germany*

*Critical Care* 2005, **9(Suppl 1):**P205 (DOI 10.1186/cc3268)

**Introduction** Severe acute pancreatitis (AP) remains associated with a high mortality. In experimental AP the application of the bovine hemoglobin solution HBOC-301 with and without IHD was able to normalize pancreatic tissue oxygen tension [1,2]. The aim of this study was to evaluate the therapeutic approach of volume therapy with HES plus HBOC-301 with and without IHD with regard to the histologic damage and survival time in pigs suffering from AP.

**Methods** After approval of the local animal ethics committee 33 pigs were anesthetized ($FIO_2$: 0.3). AP was induced by combination of cerulein and glucodeoxycholic acid. After induction of AP animals were randomized and either isovolemicly hemodiluted with 10% HES 200,000/0.5 plus HBOC-301 (+0.6 g/dl plasmatic Hb; Oxyglobin, Biopure, USA) (IHD + HBOC group) or received volume replacement without IHD with HES plus HBOC-301 (+0.6 g/dl plasmatic Hb) (HBOC group), or were hemodiluted with Ringer`s solution (IHD RINGER group) to a hematocrit (Hct) of 15%. Six hours after therapy all animals were extubated, and killed after 6 days at the latest. Two 5 µm slices from the specimens of the pancreas were examined in a blinded manner using a light microscope. The histopathologic findings were scored as previously described quantifying acinar necrosis, fat necrosis, inflammation and edema on a scale from 0 to 3 points [3]. The total score was the sum of the median of two tissue areas (maximum value 24). Statistical analyses: Kruskal–Wallis and Mann–Whitney U test ($P < 0.05$).

**Results** The histopathologic tissue damage (Table 1) was higher in the IHD RINGER group in comparison with the IHD + HBOC group and the HBOC group. The survival rate at the end of the observation period was higher in the IHD + HBOC group (10/11) and the HBOC group (8/11) in comparison with the IHD RINGER group (2/11) ($P < 0.001$).

**Table 1**

**Histopathologic score (range 0–24) of two areas from the pancreas,**

| Group | Acinar necrosis | Fat necrosis | Inflam-mation | Edema | Total score |
|---|---|---|---|---|---|
| IHD + HBOC | 3 (0–5)† | 1 (0–5) | 3 (1–4)*† | 4 (2–5) | 11 (4–17)† |
| HBOC | 3 (0–4)† | 1 (0–3)† | 4 (3–4) | 4 (2–4) | 12 (7–15)† |
| IHD RINGER | 5.5 (4–6) | 3 (1–5) | 4 (3–5) | 4 (3–5) | 16 (14–20) |

† $P < 0.05$ versus Ringer. * $P < 0.05$, IHD + HBOC group versus HBOC group.

**Implications** In a former experiment application of HBOC-301 with and without IHD normalized pancreatic tissue oxygen tensions [1]. The higher $tpO_2$ is now reflected by less tissue damage and a better outcome. The application of HBOC-301 deserves further analysis to assess its potential in the clinical treatment of AP.

**References**

1. Freitag, *et al.*: *Anesthesiology* 2004.
2. Strate, *et al.*: *Ann Surg* 1993.
3. Schmidt, *et al.*: *Ann Surg* 1992.

## P206

### Volume substitution therapy with HES 130/0.4 (Voluven®) versus HES 450/0.7 (hetastarch) during major orthopedic surgery

**S Gandhi[1], D Warltier[1], R Weiskopf[2], F Bepperling[3], D Baus[3], C Jungheinrich[3]**

*[1]Medical College of Wisconsin, Milwaukee, WI, USA; [2]University of California, San Francisco, CA, USA; [3]Fresenius Kabi, Bad Homburg, Germany*

*Critical Care* 2005, **9(Suppl 1):**P206 (DOI 10.1186/cc3269)

**Background** The first-generation hetastarch remains the only hydroxyethyl starch (HES) available for volume substitution in the United States despite its controversial safety profile. The safety and efficacy of a new HES, Voluven®, was assessed in this investigation.

**Patients and methods** After local IRB approval and signed, written informed consent, 100 adult patients scheduled for major orthopedic surgery were randomly allocated to receive 6% HES 130/0.4 (Voluven®, $n = 49$) or 6% HES 450/0.7 (hetastarch, $n = 51$) for intraoperative volume replacement in a double-blind fashion guided by a predefined algorithm that included CVP-guided therapy. HES volume served as the primary efficacy variable. Safety variables were: calculated total red blood cell (RBC) loss, minimum factor VIII activity and vW factor concentration between the end of surgery and 2 hours later, laboratory parameters, and adverse events through POD 28. The treatment groups were compared for equivalence in efficacy and superiority of HES 130/0.4 in safety.

**Results** Demographic data and other baseline characteristics of the treatment groups were similar. Mean infused HES volumes were equivalent between groups (1615 ± 778 ml for HES 130/0.4 and 1584 ± 958 ml for HES 450/0.7). Primary safety results are presented in Table 1 (mean ± standard deviation; *$P < 0.05$). Three coagulopathies were reported as serious adverse events in

**Table 1**

| | RBC loss (l) | Factor VIII (%) with >1 l HES | vW factor (%) with >1 l HES | RBC use (ml/kg) |
|---|---|---|---|---|
| HES 130/0.4 | 1.17 ± 0.63 | 88.7 ± 55.7 | 89.2 ± 40.4 | 8.0 ± 6.4 |
| HES 450/0.7 | 1.31 ± 0.84 | 65.9 ± 39.4* | 71.5 ± 36.9* | 13.8 ± 12.9* |

the HES 450/0.7 group (> 3 l HES 450/0.7 administered in all cases). No coagulopathies were reported for HES 130/0.4.

**Conclusion** HES 130/0.4 (Voluven®) and HES 450/0.7 (hetastarch) are equally effective volume expanders in major orthopedic surgery. HES 130/0.4, however, demonstrated a more favorable safety profile including preservation of critical coagulation factors and reduced requirement for transfusion of blood products.

### P207

### Sepsis Brazil — early results: albumin and mortality rate in septic shock

**C David, R Hatum, J Andrade, M Knibel, M Gomes, J Duarte, M Damasceno, P Pereira**
*Federal University of Rio de Janeiro, Brazil*
*Critical Care* 2005, **9(Suppl 1):**P207 (DOI 10.1186/cc3270)

**Introduction** The fluid replacement therapy in septic shock is a polemic issue, regarding the use of crystalloid versus colloid solutions. Albumin is the more often used colloid solution. A recently published study (SAFE study) showed no benefits in albumin versus crystalloid use, for fluid replacement in shock patients.

**Objective** To analyse the septic shock subgroup in our study, regarding the use of albumin as a fluid replacement solution and its influence on mortality.

**Patients and methods** We conducted a prospective cohort study in 50 hospitals of all regions of Brazil. The patients who were admitted or who developed sepsis during the month of September 2003 were enrolled. They were followed until the 28th day or less according to their discharge. The diagnoses were made in accordance with the criteria proposed by ACCP/SCCM. We evaluated demographic features, APACHE II, Sepsis-related Organ Failure Assessment (SOFA) score, mortality, sources of infections, microbiology and interventions. We also recorded underlying diseases and length of stay.

**Results** A total of 2419 patients were identified and 409 (16.9%) filled the criteria of sepsis, severe sepsis or septic shock. Two hundred and ten patients (51.4%) formed the septic shock subgroup, with a mean APACHE II score of 22 and a overall mortality rate of 63.8%. Eighty-five patients (40.5%) in this subgroup used albumin; 125 patients (59.5%) did not. Fifty-one patients (60%) in the albumin group died; 34 (40%) were alive on the 28th day. In the non-albumin septic shock patients subgroup, one patient (0.8%) was transferred from the hospital and excluded from the study; 83 patients (66.4%) died and 41 (32.8%) were still alive after 28 days.

When we apply the binomial probability test, the mortality rate in the albumin group is 66.93% versus 60% in the non-albumin group. Using 60% as the expected mortality rate for both subgroups (because it is the little one), $P = 0.05$. In the albumin subgroup we had 44 females and 41 males; in the non-albumin subgroup, 50 females and 75 males. The mean age and APACHE II score were the same in both subgroups (61.98 years old and 20.88, respectively).

**Conclusions** We can see a trend towards not using albumin as a fluid replacement solution in septic shock patients, a standard therapy previously. Albumin really seems not to be a protective therapy for these patients, since the mortality rate in both groups (albumin and non-albumin users) are too close (actually, when the statistical test is applied, we see a trend towards a greater mortality rate in the albumin subgroup).

### P208

### Case series of dermatomyositis complicated by acute respiratory failure requiring intensive care

**Y Teo, B Thong, D Tai, S Goh**
*Tan Tock Seng Hospital, Singapore*
*Critical Care* 2005, **9(Suppl 1):**P208 (DOI 10.1186/cc3271)

**Introduction** Dermatomyositis (DM) is a rare disorder of variable severity, ranging from mild weakness that is highly responsive to corticosteroid therapy to a relentless downhill course with pulmonary involvement that is unresponsive to all immunosuppressive modalities.

**Method** In this retrospective case series, we reviewed the clinical presentation and outcomes of all DM patients who were admitted to the medical intensive care unit (MICU) of a university-affiliated general hospital from 1 January 2000 to 31 December 2004. All had acute respiratory failure requiring mechanical ventilation (MV).

**Results** The nine patients had a mean age of 47.6 ± 12.4 (range: 27–66) years. The female to male ratio was 3.5:1. All were diagnosed to have DM before MICU admission with median duration of illness of 8 (range: 3–28) weeks. DM was classified as classical (Peter and Bohan's criteria) in six patients and amyopathic (Sontheimer's criteria) in three. Initial high-resolution computed tomography thorax in eight patients showed pulmonary fibrosis (four patients), interstitial/alveolar changes (two patients), and ground-glass changes (two patients). All patients were negative for anti-Jo1 antibody, and none had an associated malignancy.

The mean $PaO_2/FiO_2$ was 109.2 ± 40.9 (range: 61.8–181.7) mmHg. The median duration of hospital and MICU stay were 16 (range: 2–38) days and 13 (range: <1 to 37) days, respectively. The median duration of MV was 10 (range: <1 to 37) days.

All chest radiographs showed bilateral lung infiltrates. Broncho-alveolar lavage was performed on six patients, with findings of pneumocystis cariini in one patient and mycobacterium tuberculosis in another. All patients were treated empirically with broad-spectrum antibiotics for pneumonia including cotrimoxazole for *Pneumocystis carinii* on admission to the MICU. Immuno-suppressive therapies in the MICU included high-dose systemic corticosteroids in all, pulse methylprednisolone (five patients), pulse cyclophosphamide (three patients), high-dose intravenous immunoglobulin (one patient) and cyclosporine (two patients). All patients died of respiratory failure with four having hypotension and acute renal failure as contributing causes.

**Conclusion** DM with pulmonary involvement that required MV carries an extremely high mortality. Early diagnosis and effective immunosuppressive therapies for lung disease may help to improve outcome in this high-risk group.

### P209

### Outcome following burns from 1985 to 2004 in the Centre for Severely Burned Patients, Ghent University Hospital, Belgium

**N Brusselaers, E Hoste, K Vandewoude, J De Waele, K Colpaert, S Monstrey, S Blot**
*University of Ghent, Belgium*
*Critical Care* 2005, **9(Suppl 1):**P209 (DOI 10.1186/cc3272)

**Background** Mortality in burn patients can be estimated by three major risk factors for death: age > 60 years, total burned surface

area (TBSA) > 40% and presence of an inhalation injury [1]. The formula developed by Ryan predicts 0.3%, 3%, 33% and 90% mortality when zero, one, two or three risk factors are present.

**Objective** A retrospective evaluation of the prognostic value of these three risk factors in patients admitted to our burn unit over a 20-year period (May 1985–November 2004) ($n = 1385$).

**Results** Mean age was 32 ± 23 years. The mean %TBSA was 19 ± 18%. Inhalation injury was present in 166 patients (12%). Overall mortality was 7%. When zero, one, two or three risk factors were present, mortality was respectively 0.5%, 10%, 48% and 91%. Risk factors and related mortality rates are presented in Table 1.

**Table 1**

| Risk factors (*n*) | Age | TBSA > 40% | Inhalation injury | Mortality (%) | Ryan mortality (%) |
|---|---|---|---|---|---|
| Zero | – | – | – | 5/998 (0.5) | 4/1314 (0.3) |
| One | + | – | – | 13/133 (9.8) | 4/75 (5) |
| One | – | + | – | 5/82 (6.1) | 1/31 (3) |
| One | – | – | + | 8/49 (16.3) | 5/112 (4) |
| Two | + | + | – | 4/6 (66.7) | 0/1 (0) |
| Two | + | – | + | 13/19 (68.4) | 12/39 (39) |
| Two | – | + | + | 32/77 (41.6) | 21/79 (27) |
| Three | + | + | + | 19/21 (90.5) | 21/22 (95) |

**Conclusion** Global mortality following burns is low. Nearly all patients who died had at least one risk factor present. Given the broad classes of this classification and the differences in age and %TBSA between Ryan's study and our population, this model predicts mortality in a reliable but very coarse way.

**Reference**

1. Ryan, *et al.*: *N Engl J Med* 1998, **338:**362-366.

## P210

### A retrospective cohort study of 36-month use of paediatric intensive care and associated mortality in Sweden

**H Kalzen[1], N Gullberg[2], O Luhr[1], S Gothberg[3], A Olsson[4], O Winso[5], A Markstrom[1], C Frostell[2]**

*[1]Karolinska Institute Danderyd Hospital, Stockholm, Sweden; [2]Karolinska University Hospital, Stockholm, Sweden; [3]Sahlgrenska University Hospital, Gothenburg, Sweden; [4]Lund University Hospital, Lund, Sweden; [5]Scandinavian Critical Care Trials Group, Umea, Sweden*

*Critical Care* 2005, **9(Suppl 1):**P210 (DOI 10.1186/cc3273)

**Background** To determine mortality for children, aged 6 months–16 years, treated in pediatric intensive care units (PICUs) or adult intensive care units (AICUs) or transferred from AICU to PICU in Sweden.

**Methods** A retrospective, multicentre, 3-year cohort study. Name, social security number, admission and discharge dates were collected from March 1998 to March 2001, after securing ethics committee approval. Using the national files of registration, mortality could be assessed.

**Results** Fifty-five of 75 AICUs and all PICUs ($n = 3$) generated data. A total of 5757 patients (male/female 1.3:1) were admitted, estimated as > 90% of all patients of this period. A total of 1985 patients were primarily admitted to PICUs and 3772 patients to AICUs. Of the latter, 90 patients were transferred. The 1-year mortality for patients in AICUs, in PICUs or transferred was 2.8% ($n = 110$), 3.6% ($n = 72$) and 12% ($n = 11$). Mean length of stay was 1 day in both ICU groups. Accountable days in ICUs was 6370.

**Table 1**

| | |
|---|---|
| AICU | |
| Total number | 3772 |
| ICU deaths | 53 |
| Additional deaths up to 3 years | 86 |
| Late mortality, > 3–6.5 years | 21 |
| PICU | |
| Total number | 1985 |
| ICU deaths | 29 |
| Additional deaths up to 3 years | 83 |
| Late mortality, > 3–6.5 years | 23 |

**Conclusion** Overall 1-year mortality was relatively low (< 4%) (male = female). However, we noted an elevated risk of death beyond 3 years after discharge. The higher mortality in the small transferred group could reflect a lack of available PICU beds. Based on these figures six beds, with 100% usage, would meet the total requirement of ICU beds for this age range in Sweden.

## P211

### Significant ICU respiratory morbidity in postoperative patients with adult congenital heart disease

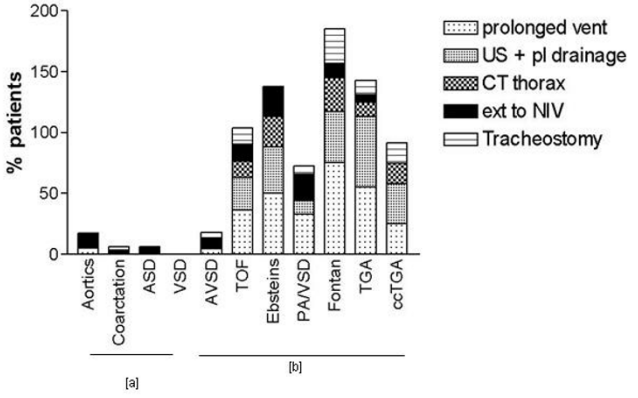
**S Price, S Trenfield, S Jagger, S Jordan, T Evans**

*Royal Brompton Hospital, London, UK*

*Critical Care* 2005, **9(Suppl 1):**P211 (DOI 10.1186/cc3274)

**Introduction** Increasing numbers of patients with congenital heart disease now survive to adulthood, requiring repeated surgical and cardiological interventions that necessitate ICU admission [1]. There are little data in the literature regarding the ICU morbidity and mortality in this patient population. We therefore evaluated the ICU respiratory morbidity in patients with adult congenital heart disease (ACHD).

**Figure 1 (abstract P211)**




Prolonged vent, prolonged ventilation > 72 hours; US+pl drainage, ultrasound and pleural drainage; CT thorax, computerised tomography thorax; ext to NIV, extubation to non-invasive ventilation and tracheostomy; ASD, atrial septal defect; VSD, ventricular septal defect; AVSD, atrioventricular septal defect; TOF, Tetralogy of Fallot; TGA, transposition of the great arteries.

**Methods** A database (Medicus, High Wycombe, UK) was interrogated for all patients admitted to the ICU of a cardiothoracic tertiary referral centre during the period January 1997–2002 with ACHD. Classification of ACHD complexity was according to the modified Canadian Consensus Conference criteria. Patient demographics, details of any surgical procedure and mortality were extracted. Analysis of respiratory investigations and interventions (Fig. 1) was performed.

**Results** Over the accounting period 342 patients with ACHD were admitted (6.4% of total ICU admissions), of which 305 (90%) were following cardiac surgery. Perioperative mortality was 3.3%. Patients with simple ACHD had zero mortality, a low requirement for respiratory investigations and interventions (Fig. 1a). Patients with moderately complex and complex ACHD had a higher mortality (10.6%) and significantly higher requirement for respiratory investigations and interventions (Fig. 1b).

**Conclusion** Patients undergoing surgery for complex ACHD have a significant requirement for respiratory investigations and interventions. As the case mix is changing, with more complex patients requiring intervention in adulthood, this has implications for future planning of ICU ACHD care.

**Acknowledgement** SP is the BHF Jill Dando Adult Congenital Cardiology Fellow.

**Reference**

1. Somerville J: **Management of adults with congenital heart disease: an increasing problem.** *Annu Rev Med* 1997, **48:**283-293.

## P212

### Intensive care in adults with congenital heart disease: cost implications of a changing patient population

**S Price, S Trenfield, S Jagger, S Jordan, T Evans**
*Royal Brompton Hospital, London, UK*
*Critical Care* 2005, **9(Suppl 1):**P212 (DOI 10.1186/cc3275)

**Introduction** Current estimations suggest there are around 800,000 patients in the USA with congenital cardiac lesions requiring specialist care [1]. Improved surgical and cardiological interventions mean that numbers of patients with moderate-severe congenital lesions will increase [2], resulting in increased requirement for repeat surgery in adulthood. This is reflected by an increasingly complex case mix requiring ICU admission. The potential impact of this changing patient population upon ICU resources has not been addressed.

**Methods** A database (Medicus, High Wycombe, UK) was interrogated for all patients admitted to the ICU during the period January 1997–2002 with adult congenital heart disease (ACHD), which was classified as simple or complex according to the modified Canadian Consensus Conference criteria. Patient demographics, the length of ICU stay (LOS) and mortality were extracted, and the severity of illness and intensity of intervention calculated (APACHE II, TISS-28).

**Results** Of 5312 patients admitted during the accounting period, 342 had ACHD (6.4%). ACHD ICU mortality was 4.4%. Patients with simple ACHD (32%) had APACHE II scores of 18.4 ± 4.8, zero mortality, short LOS (1.8 ± 2 days), and low therapeutic intervention (TISS-28 42.3 ± 10). Patients with complex ACHD (68%) had similar APACHE II scores (18.5 ± 6.4, not significant) but significantly higher mortality (10.6%), increased LOS (3.9 ± 2 days, $P < 0.05$) and requirement for intervention (TISS-28 59.8 ± 13, $P < 0.05$). Overall mean cost per admission (TISS score point 46.31, €67.0) was therefore significantly higher in the more complex patients (simple €5101 ± 1340 vs complex €15,623 ± 1742, $P < 0.05$).

**Conclusion** Improved survival of patients with complex congenital heart disease to adulthood will have significant implications (clinical and financial) in any ICU undertaking this work.

**Acknowledgement** SP is the British Heart Foundation Adult Congenital Cardiology Fellow.

**References**

1. Warnes CA, Liberthson R, Danielson GK, Dore A, Harris L, Hoffman JI, Somerville J, Williams RG, Webb GD: **Task force 1: the changing profile of congenital heart disease in adult life.** *J Am Coll Cardiol* 2001, **37:**1170-1175.
2. Wren C, O'Sullivan JJ: **Survival with congenital heart disease and need for follow up in adult life.** *Heart* 2001, **85:**438-443.

## P213

### HELLP syndrome: analysis of 23 cases

**C Kaddour, M Laamourou, R Souissi, Z Haddad, T Chaaoua, H Ouragini, W Gdoura**
*National Institute of Neurology, Tunis, Tunisia*
*Critical Care* 2005, **9(Suppl 1):**P213 (DOI 10.1186/cc3276)

**Context** HELLP syndrome (hemolysis, elevated liver enzymes, low platelets) is a severe complication in late pregnancy. This disorder complicates between 2% and 7% of gestations and is associated with a high maternal morbidity ranging between 1% and 4%.

**Objective** We undertook this study to evaluate the repercussions on maternal outcome in patients with HELLP syndrome and to determine its clinical and biological characteristics.

**Design** A retrospective and analytical study.

**Setting** The intensive care unit of the National Hospital of Neurology, Tunisia.

**Sample** Pregnant or postdelivery women who had HELLP syndrome between January 1996 and December 2003.

**Main measurements** Analysis was made of maternal age, parity, hypertension classification, gestational age at HELLP syndrome diagnosis, alterations in laboratory test for HELLP syndrome, time elapsed to discharge from hospital, maternal complications and mode of delivery.

**Results** Twenty-three patients with HELLP syndrome were selected. Mean age was 33 (26–40) years. The mean gestation was 32 weeks, and 85% were delivered by caesarean section. One patient had postpartum HELLP syndrome. Hypertension was observed in all cases. Twenty-two women needed blood product transfusions. A nadir platelet count of 50,000/µl was not an independent risk factor for adverse outcome. The main complication was acute renal failure. Five patients died; three of them had a cerebral hemorrhage.

**Conclusion** The high maternal morbid–mortality of HELLP syndrome requires management in a center where intensive maternal care is available.

## P214

### Critically ill severe pre-eclamptic patients admitted to an obstetric intensive care unit

**W Teoh[1], H Neo[1], I Tan[2]**
*[1]KK Women's & Children's Hospital, Singapore; [2]Singapore General Hospital, Singapore*
*Critical Care* 2005, **9(Suppl 1):**P214 (DOI 10.1186/cc3277)

**Objective** To profile severe pre-eclamptic (SPE) patients admitted to an obstetric ICU, with regards to manifestations, interventions and clinical outcome.

**Methods** Medical records of all SPE patients admitted from 2002 to 2004 to our ICU were retrospectively analysed.

**Results** One hundred and four patients with SPE were admitted, 89% postpartum. This represents 38.5% of all obstetric admissions to the ICU, and 0.23% of all deliveries in our hospital, during the same period.
All except five patients (4.8%) received antenatal care, of which 40.4% were known pre-eclamptics on medication. The mean gestational age at detection of SPE was 32.5 (0.4) weeks, with a mean arterial pressure of 129.2 (1.7) mmHg.
Reasons for ICU admission in addition to SPE included pulmonary edema (14.4%), oliguria (14.4%), hemolysis elevated liver enzymes low platelet (HELLP) syndrome (18.3%), eclampsia (7.7%), and intracerebral hemorrhage (1%). The incidence of eclampsia was 1.7 per 10,000 births.
Arterial lines were inserted in 64.4% and central venous catheters in 18% of patients. Magnesium sulphate therapy was instituted in 69.2% of patients for a mean duration of 28.7 (2.6) hours. Forty-seven percent of patients received intravenous and oral antihypertensives, while 45% required oral antihypertensives only. Nine patients (8.6%) received invasive mechanical ventilation for 29.6 (13.4) hours, and three patients (2.9%) required renal replacement therapy.
The mean ICU length of stay was 46.5 (2.0) hours. Indications for delivery in addition to SPE were worsening maternal biochemical indices (42.3%), fetal distress (18.3%), pulmonary edema (11.5%), impending eclampsia (16.3%), and eclampsia (3.8%). Delivery was by emergency Caesarean section in 90.4%, and vaginal delivery in 9.6%. Mean gestational age at delivery was 33.2 (0.4) weeks, with birthweight 1894 (81) g, and mean Apgar score of 7 at 1 min, and 8 at 5 min. A total 14.4% of babies were small for gestational age, and four perinatal mortalities occurred (0.09 per 1000 births). There were only two maternal deaths (0.04 per 1000 deliveries).
**Conclusion** SPE is a prevalent cause of maternal–fetal morbidity. With improved obstetric and intensive care, the current incidence of eclampsia (1.7 per 10,000 births) is one of the lowest in published literature for a tertiary referral maternity hospital.

## P215

## Nursing workload and prognosis in the critically ill obstetric patient

**Z Haddad, C Kaddour**
*National Institute of Neurology, Tunis, Tunisia*
*Critical Care* 2005, **9(Suppl 1):**P215 (DOI 10.1186/cc3278)

**Introduction** A critically ill obstetric patient usually recovers rapidly after delivery, resulting in a short length of stay (LOS), with a reduced number of specific interventions in the ICU and a good overall prognosis. Some authors therefore stated a possible management of these patients on the delivery/labor floor or in high dependency units.
**Objective** To measure nursing workload with the NEMS score [1], evaluate whether management in the ICU was required (NEMS > 20) and correlation with mortality.
**Design** A retrospective chart review study.
**Setting** An independent multidisciplinary ICU in a tertiary university hospital.
**Study period** January 1996–June 2004.
**Patients** All obstetric patients ($n = 590$) admitted to the ICU.
**Measurements and results** Forty-nine patients were excluded due to insufficient data. Mean NEMS was 27.1 ± 6.75 with values ranging from 18 to 50. Mean NEMS for survivors was 25.8 ± 5.19, mean NEMS for nonsurvivors was 37.75 ± 8.78 ($P < 0.001$). A total 21.6% ($n = 117$) of our patients got a NEMS score < 20 (mean 18), among them 18 patients (15.4%) either increased their NEMS the next day and then died, or lasted with the same NEMS for a few days.
NEMS_H24 discriminated well with an AUROC of 0.855 ± 0.072, but calibrated badly (Pr < 0.001). Also NEMS_H48 (after excluding patients with LOS < 2 days) discriminated well (AUROC = 0.977), and calibrated better than NEMS_H24 but still insufficiently (Pr = 0.02).
**Conclusion** According to the NEMS score 81.7% of our patients deserved to be hospitalized in the ICU. NEMS_H24 and NEMS_H48 correlated with mortality. Fifteen percent of patients with initial NEMS < 20 needed intensive monitoring for more than 1 day, and five patients died. We suggest a large admission policy to a multidisciplinary ICU be encouraged for obstetric patients, because monitoring is better and treatment of possible late complications occurs earlier, a sole guarantee to reduce mortality.

**References**

1. R Moreno, DR Miranda: **Nursing staff in intensive care in Europe. The mismatch between planning and practice.** *Chest* 1998, **113:**752-758.

## P216

## Pre-eclampsia in the intensive care unit: indicators of severity and hospital outcome

**I Gouveia, C Costa, P Cunha, A Bártolo, R Milheiro, C Gonçalves, A Carvalho, T Cardoso, S Martins, J Magalhães**
*HSO, Guimarães, Portugal*
*Critical Care* 2005, **9(Suppl 1):**P216 (DOI 10.1186/cc3279)

**Introduction** Pre-eclampsia is a disease unique to pregnancy that is often associated with significant maternal morbidity and mortality, especially when it is severe. The aim of this study was to evaluate which indicators of severe pre-eclampsia were among the reasons for ICU admission and their impact on the length of hospital stay.
**Materials and methods** We used a computerized database to identify 444 women with pre-eclampsia–eclampsia among 32,382 deliveries from 1996 to 2003 in our institution. Of these, 24 women were admitted to the ICU because of severe pre-eclampsia and were retrospectively included in our study. Maternal demographic data included age, parity and medical history. Gestational age, mode of delivery, days staying in the ICU and in the ward, outcome of ICU admission and SAPS II score were record for each patient. Indicators of severe pre-eclampsia on admission to the ICU included a sustained BP of 160/110 mmHg or more, proteinuria 4+ on qualitative assessment, oliguria (< 20–30 ml/hour), renal insufficiency (creatinine level >1.3 mg/dl), elevated liver enzymes, low platelet count (<100,000/µl), positive testing for hemolysis, epigastric pain, headache, visual disturbances and seizures. In the statistical analysis we used the *t* test on SPSS®. Data were considered significant when $P < 0.05$.
**Results** The mean maternal age was 29 years. Twelve women were nulliparous (50%). No women had history of chronic hypertension. All 24 women underwent a cesarian delivery because of severe pre-eclampsia at > 20 weeks of gestation, except for one woman with pregnancy of 16 weeks. All 24 women had at least one indicator of severity on admission to ICU that included BP ≥ 160/110 mmHg ($n = 13$), elevated liver enzymes ($n = 13$), low platelet count ($n = 12$), oliguria ($n = 11$), headaches ($n = 8$), epigastric pain ($n = 7$), seizures ($n = 6$), renal insufficiency ($n = 2$) and hemolysis ($n = 2$). The mean SAPS II score was 15. Complications occurred in eight women. None of the women died. The average length of stay was 3 days in the ICU and 10 days in the ward. Indicators of severity related to longer hospital stay were seizures ($P = 0.002$), epigastric pain ($P = 0.004$) and oliguria ($P = 0.004$). No significant difference was found regarding other severity indicators, SAPS II score and development of complications.

**Conclusions** Our results have limited significance mainly because of the sample size ($n = 24$). However, they may potentially guide intensive care of these patients in order to shorten hospital stay and reduce inherent morbidity and costs. Intensivists as well as obstetricians should work closely toward this purpose.

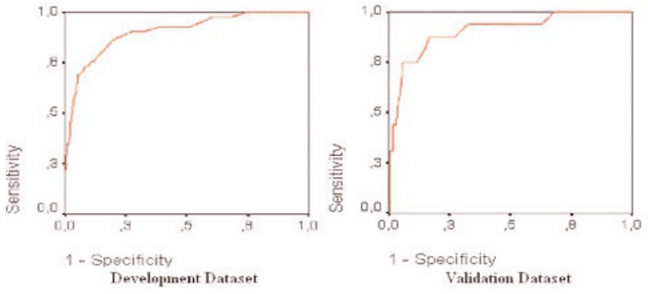
## P217

### Development and validation of a new scoring system for the critically ill obstetric patient

**Z Haddad[1], C Kaddour[1], T Chaaoua[1], M Laamourou[1], O Kaabachi[1], R Souissi[1], S Nagi[1], L Skandrani[1], J Golmard[2]**
*[1]National Institute of Neurology, Tunis, Tunisia; [2]University of Medecine Pitié Salpêtrière, Paris, France*
*Critical Care* 2005, **9(Suppl 1):**P217 (DOI 10.1186/cc3280)

**Introduction** Measuring physiological status prior to ICU admission could help refine prognosis after ICU discharge. The literature lacks such studies.
**Objective** To determine the correlation between a New Simplified Acute Physiology Score designed for obstetric patients before their admission to the ICU and ICU mortality.
**Design** A prospective study, part of the Assessment of Prognosis and Risk of Mortality in Obstetrics (APRiMO) study. Seventeen physiologic and biologic parameters were measured, and pathological intervals shifted to fit physiologic changes related to pregnancy as described by Margaria [1] with a slight modification. An aggregate score included the worst value for each parameter during a maximum of 24 hours before admission to the ICU. Patients were devided into two datasets: development ($n = 350$) and validation ($n = 191$). Discrimination was assessed by the area under the receiver operator characteristic curve (AUROC). Calibration was assessed by Hosmer–Lemeshow (Pr) goodness-of-fit C statistics. After validation of the overall score, we tried to simplify it without altering its statistical power. Statistical analysis was computed on SPSS 11.5 XP-Windows compatible. $P < 0.05$ was considered significant. Results are expressed by mean ± standard deviation.
**Setting** Patients were first managed in a tertiary care obstetric hospital, a referral center for high-risk pregnancies, with a level 3 neonatal ICU. Then they were transferred to our independant multidisciplinary ICU.
**Study period** January 1996–December 2003.
**Patients** All obstetric patients ($n = 541$) transferred to the ICU. Inclusion criteria: severe pre-eclampsia/eclampsia, HELLP syndrome, stroke, and so on.
**Measurements and results** Obstetric complications accounted for 70% of admissions. Mean age was 31.2 ± 5.9 years, Mean term was 34.7 ± 4.5 weeks. The majority of our patients were admitted after delivery. The mortality rate was 10.4% ($n = 57$). In the development dataset, the SAPS-O discriminated (AUROC = 0.902) and calibrated (Pr = 0.524) well. The validation dataset also discriminated (AUROC = 0.904) and calibrated (Pr = 0.895) well (Fig. 1). A simplified model made with 7/17 parameters also discriminated and validated well with, respectively, AUROC and Pr in the same development and validation data of: AUROC 0.947 and 0.793; Pr 0.968 and 0.716.
**Conclusion** SAPS-O is correlated to ICU prognosis. This could help adjust for lead-time bias, comparison between centers and management policies.

**Figure 1 (abstract P217)**




**Reference**

1. Margaria E, Collo E, Castelli I: **Which patients must be admitted to the intensive care unit.** *Anesthésie-Réanimation en obstétrique*. Editions Arnette JEPU; 1994.

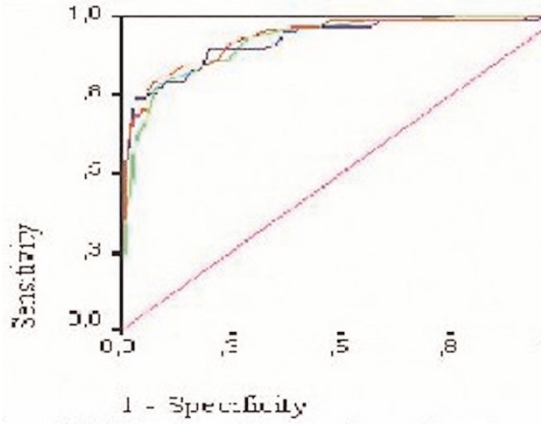
## P218

### Critically ill obstetric patients: outcome and predictability

**Z Haddad[1], J Golmard[2], C Kaddour[3], M Laamourou[3], R Souissi[3], T Chaaoua[3], O Kaabachi[3], S Nagi[3], L Skandrani[3]**
*[1]Neurochirurgie, Paris, France; [2]Pitié-Salpêtrière University of Medecine, Paris, France; [3]National Institute of Neurology, Tunis, Tunisia*
*Critical Care* 2005, **9(Suppl 1):**P218 (DOI 10.1186/cc3281)

**Introduction** Outcome prediction in the critically ill obstetric patient is controversial.
**Objective** To determine the applicability of SAPS II, APACHE II and APACHE III-J scores calculated at day 1 of admission in outcome prediction.
**Design** An open prospective data collection, as part of the Assessment of Prognosis and Risk of Mortality in Obstetrics (APRiMO) study. Discrimination was assessed by area under the receiver operator characteristic curve (AUROC). Calibration was assessed by Hosmer–Lemeshow (HL) C statistic. $P < 0.05$ was considered significant.
**Setting** A multidisciplinary ICU.
**Study period** January 1996–December 2003.
**Patients** Obstetric patients ($n = 541$) admitted for at least 4 hours in the ICU.
**Measurements and results** Mean age was 31.2 ± 5.9, mean term was 34.7 ± 4.5 weeks. Seventy percent of admissions were

**Figure 1 (abstract P218)**




Receiver operator characteristic curves of the severity scoring systems' admissions.

obstetric complications. The mortality rate was 10.4% ($n = 57$). The three scores discriminated (Fig. 1) and calibrated (Table 1) well. APACHE III was the only score to calibrate well using original mortality prediction equations (Table 2).

**Table 1**

| Scoring system | Survivors | Non-survivors | AUROC | HL C statistics | SMR |
|---|---|---|---|---|---|
| SAPS II | 20.35 | 55.7 | 0.926 ± 0.04 | 0.399 | 0.96 |
| APACHE II | 7.07 | 21.2 | 0.918 ± 0.035 | 0.653 | 1.06 |
| APACHE III | 23.1 | 81.97 | 0.917 ± 0.045 | 0.73 | 1.43 |

**Table 2**

| Scoring system | AUROC | HL C statistics |
|---|---|---|
| SAPS II | 0.925 | 0.036 |
| APACHE II | 0.785 | 0.02 |
| APACHE III | 0.922 | 0.15 |

**Conclusion** The three scores are good discriminators. Customization of the mortality prediction equations seems necessary. APACHE III-J seems to be the best (adjustment by adequate diagnostic categories).

## P219

### Case mix outcome and activity for patients with ARF during the first 24 hours of the intensive care unit

**P Stevens[1], A Slack[1], A Crowe[2], G Lipkin[3], A Brady[4], D Harrison[4]**
*[1]Kent and Canterbury Hospital, Canterbury, UK; [2]Countess of Chester Hospital, Chester, UK; [3]Queen Elizabeth Hospital, Birmingham, UK; [4]ICNARC, London, UK*
*Critical Care* 2005, **9(Suppl 1):**P219 (DOI 10.1186/cc3282)

We examined outcomes for patients with ARF identified from a national comparative audit of adult general ICUs in England, Wales and Northern Ireland, the Case Mix Programme.
Of 276,731 admissions to 170 ICUs over an 8-year period ARF was present during the first 24 hours of admission in 17,326 (6.3%), 66% were male. Oliguria and non-oliguria were determined by UOP < 400 ml/day or > 400 ml/day. Table 1 presents age, surgical status and mortality of the ARF patients. Mean APACHE II score was 24.8 compared with 16.5 for all ICU admissions, and was significantly higher in oliguric ARF (29.3) versus non-oliguric (17.9). A total of 83.7% of admissions with ARF were non-surgical. Both ICU and hospital mortality were significantly higher for oliguric ARF compared with non-oliguric ARF. Factors predicting increased mortality were: increasing age, male sex, chronic conditions, CPR, IPPV, oliguria, prior hospital stay of 7+ days, extremes of temperature, heart rate and respiratory rate, low MAP, low pH, high A-a$DO_2$, abnormal sodium, high potassium, low albumin, low WBC and low Glasgow Coma Score. Surgery within 1 week of ICU admission conferred survival benefit.
The median ICU length of stay (LOS) was 4.1 days for ARF survivors and 2.0 days for non-survivors, compared with 1.7 and 2.0 days, respectively, for all ICU admissions. Admissions with ARF accounted for 9.3% of all ICU bed days. Median hospital LOS was 31 days for ARF survivors and 8 days for non-survivors, compared with 16 and 9 days, respectively, for all ICU admissions. Oliguria was associated with longer LOS for survivors and shorter LOS for non-survivors.

**Table 1**

| | All ARF | Oliguric | Non-oliguric |
|---|---|---|---|
| Number | 17,326 | 5687 | 10,133 |
| Mean age, years | 63.2 | 63.5 | 63.1 |
| Non-surgical | 14,479 | 5005 | 8125 |
| Elective surgery | 961 | 187 | 717 |
| Emergency surgery | 1868 | 487 | 1280 |
| ICU mortality | 7508 (43.3%) | 3176 (55.8%) | 3387 (33.4%) |
| Hospital mortality | 9725 (58.6%) | 3850 (70.3%) | 4770 (49.3%) |

Although the predominant cause of ICU ARF is now non-surgical the factors influencing survival remain unchanged. ARF occupies ca. 10% of all ICU bed days and doubles both ICU and hospital LOS in survivors.

## P220

### Factors predictive of mortality and mortality prediction models in patients with ARF during the first 24 hours of intensive care unit admission

**A Slack[1], P Stevens[1], G Lipkin[2], A Crowe[3], A Brady[4], D Harrison[4]**
*[1]Kent and Canterbury Hospital, Canterbury, UK; [2]Queen Elizabeth Hospital, Birmingham, UK; [3]Countess of Chester Hospital, Chester, UK; [4]ICNARC, London, UK*
*Critical Care* 2005, **9(Suppl 1):**P220 (DOI 10.1186/cc3283)

We examined outcomes for patients with ARF identified from a national comparative audit of adult general ICUs in England, Wales and Northern Ireland, the Case Mix Programme.
Over an 8-year period ARF was present during the first 24 hours of admission in 17,326 of 276,731 admissions to the ICU. In 14,118 (81.5%) sufficient data were present to predict mortality using the Stuivenberg Hospital ARF (SHARF), UK APACHE II, and Mehta mortality prediction models. Discrimination was assessed by the area under the receiver operating characteristic curve (ROC), calibration by the mortality ratio (observed versus predicted mortality), and overall fit by the *R*-statistic from Shapiro's Q representing the geometric mean of the probability assigned to the true outcome.
Factors predicting > 50% increased mortality risk were: history of chronic condition, CPR, IPPV, oliguria, prior hospital stay of 7+ days, MAP < 50 mmHg, acidosis, and reduction of GCS by 2. UK APACHE II scores showed the best discrimination and calibration, although the null hypothesis of perfect calibration was strongly rejected ($P < 0.001$) by both the Hosmer–Lemeshow test and Cox's calibration regression. UK APACHE II and Mehta underpredicted the number of deaths while SHARF T0 overpredicted (Table 1). SHARF T0 and Mehta's model showed poor overall fit by Shapiro's Q, with an $R$ value < 0.5.

**Table 1**

| | SHARF T0 | MEHTA | UK APACHE II |
|---|---|---|---|
| Discrimination | AUC 0.632 | AUC 0.693 | AUC 0.740 |
| Calibration | MR 0.759 | MR 1.223 | MR 1.147 |
| Fit, Shapiro's Q | $R = 0.392$ | $R = 0.487$ | $R = 0.539$ |

AUC, area under the ROC curve; MR, mortality ratio.

Although UK APACHE II scores performed best, none of the existing mortality prediction models reliably predict those who will survive to leave hospital following an episode of ARF in the ICU. Traditional risk factors such as oliguria, CPR, LOS > 7 days prior

to admission to ICU and extremes of physiology continue to be associated with the greatest increased risks of mortality.

### P221

### Mortality and predictors of death in patients with pneumonia admitted to the intensive care unit

**J Lee, Y Ryu, E Cheon, J Chang**
*Ewha Womans University Hospital, Seoul, South Korea*
*Critical Care* 2005, **9(Suppl 1):**P221 (DOI 10.1186/cc3284)

**Background** Community-acquired pneumonia remains a common and serious condition.
**Methods** We retrospectively evaluated patients with pneumonia admitted to the medical intensive care unit (MICU) of Ewha Womans University Hospital from 1 January 2000 through 31 December 2003. We excluded patients who died within 48 hours after admission, were pretreated before admission or had pulmonary tuberculosis or suspected nosocomial pneumonia. Finally, 118 patients were included.
**Results** Mortality was 41.5% (49/118). At admission, survivors had significantly higher white blood cell counts ($P < 0.05$), lower serum potassium levels ($P < 0.05$), larger first 24-hour urine output ($P < 0.01$), higher Glasgow coma scales ($P < 0.001$), and lower Acute Physiology and Chronic Health Evaluation Score (APACHE II) ($P < 0.01$) than non-survivors. During hospitalization, there was significantly lower incidence of gastrointestinal (GI) bleeding in survivors compared with non-survivors ($P < 0.001$). MICU stay ($P < 0.05$) and days requiring mechanical ventilation ($P < 0.001$) and intubation were significantly shorter in survivors compared with those in non-survivors ($P < 0.01$). Tracheostomy was less frequently performed in survivors compared with that in non-survivors ($P < 0.01$). In survival analysis using Cox regression, GI bleeding (relative risk [RR], 2.35; 95% confidence interval [CI], 1.24–4.48) and an APACHE II score of 20 or more (RR, 2.19; 95% CI, 1.21–3.96) were independently associated with death.
**Conclusion** In patients with severe pneumonia, mortality was still high. GI bleeding during hospitalization as well as high APACHE II score was related to mortality.

### P222

### Survival and prognosis after assisted ventilation for acute respiratory failure in cystic fibrosis

**S van Gestel[1], M Slieker[1], G Tramper[1], F Teding van Berkhout[2], H Heijerman[3], K van der Ent[1], K Jansen[1]**
*[1]UMC Utrecht, Wilhelmina Children's Hospital, Utrecht, The Netherlands; [2]UMC Utrecht, The Netherlands; [3]Leyenburg Hospital, The Hague, The Netherlands*
*Critical Care* 2005, **9(Suppl 1):**P222 (DOI 10.1186/cc3285)

**Introduction** The use of mechanical ventilation for acute respiratory failure (ARF) in patients with cystic fibrosis (CF) has long been discouraged because of a poor outcome in this group of patients. However, new insights into ventilatory strategies and a better life expectancy *per se* in CF patients necessitate regular re-evaluation of this attitude. The most recent studies report a mortality in adult CF patients requiring mechanical ventilation that varies widely between 45% and 80%. Results in children are reported as more favourable, but little is known about the long-term pulmonary outcome of children with CF who required mechanical ventilation for ARF already at a young age.
**Objectives** The goals of this study were threefold: to assess outcome of assisted ventilation in CF patients with ARF; to identify risk factors associated with a poor outcome; and to analyse whether children with CF who required mechanical ventilation for ARF at a young age had more pulmonary and CF-related complications later in life compared with unventilated CF controls.
**Design** A retrospective cohort study.
**Setting** The study was performed at the University Medical Centre Utrecht (Utrecht, The Netherlands) and at the Leyenburg Hospital (The Hague, The Netherlands). These centres care for approximately one-half of the Dutch CF population.
**Methods** Medical charts were reviewed of all CF patients who had been admitted to the intensive care unit for ARF between January 1990 and August 2003. ARF was defined as a respiratory deterioration requiring assisted ventilation, due to an acute illness in a previously stable patient. Assisted ventilation could be either non-invasive or invasive. Patients with chronic respiratory failure with a slow progressive decline in lung function were not included. To identify risk factors for mortality, the following data were recorded: demographic data, body mass index, spirometric data, mode of ventilation, sputum microbiology, history of hemoptysis or pneumothorax, the presence of CF-related diabetes and the presence of CF-related liver disease.
To analyse long-term outcome in children who survived assisted ventilation for ARF, all unventilated age-matched and gender-matched CF controls were identified. Lung function and the presence of CF-related complications 5 years after admission to the ICU were compared.
**Results** Thirty-two CF patients were included, five children (aged 2–18 months) and 27 adults (aged 15 years and older). All children and 30% of the adults survived.
In the total population, age was a statistically significant risk factor for poor outcome ($P = 0.03$). In the adult population, none of the demographic and clinical data could predict outcome significantly. In patients who had an episode of ARF in childhood, clinical course and lung function 5 years after assisted ventilation was not significantly different compared with their controls.
**Conclusions** CF patients aged 2 years or younger who are ventilated because of ARF have a good prognosis and assisted ventilation does not seem to affect lung function or development of CF-related complications later in their lives. ARF in adult CF patients still is associated with a high mortality. Risk factors for poor outcome could not be identified.

### P223

### Outcome of septic shock in patients with malignancies and neutropenia

**D Furmanchuk**
*Belorussian Medical Academy for Postgraduate Education, Minsk, Belarus*
*Critical Care* 2005, **9(Suppl 1):**P223 (DOI 10.1186/cc3286)

**Background** Septic complication remains an important influence on survival rate in patients with malignancies. Bone marrow suppression and neutropenia induced by chemotherapy determine certain difficulties in early diagnose of sepsis, and lead to rapid hemodynamics and respiratory disorders. The aim of this study was to standardize most important issues in treatment of sepsis-induced arterial hypotension and tissue hypoperfusion and to estimate its influence on survival rate in patients with severe sepsis and septic shock.
**Materials and methods** Sixty-two consecutive patients aged from 1 to 17 years old, with malignancies, neutropenia and sepsis associated with hypotension, were followed in the ICU of the Republican Center for Pediatric Oncology and Hematology. Thirty-five patients treated from January 2000 to December 2001

composed the retrospective group; the prospective group consisted of 27 patients, treated from March 2003 to September 2004. Treatment protocol for septic shock therapy used EBM principles and the design for the prospective group strictly determined the following treatment options: hydroxyethyl starch (HES) as a first choice for volume resuscitation; combination of dopamine and norepinephrine for correction of arterial hypotension; double-lumen catheter (or two central lines) for dividing infusions of dopamine and noradrenalin from others; mandatory use of arterial lines for invasive blood pressure monitoring; and start-up of mandatory ventilation in all patients with septic shock, even in patients with compensated blood gas status,
We compared the survival rate and survival probability during the first 75 days after ICU admission. For the statistical analysis, the chi-square test and the Caplan–Meyer method were used.
**Results** Survival probability measured by log-rank test during 75 days after ICU admission showed a significant difference. Using our protocol, we also found a difference in maximal lactate level on the day of admission, duration of arterial hypotension, length of ICU stay and length of ventilation between two groups.
The overall ICU mortality rate was significantly different in the retrospective and prospective groups – 81.3% and 53%, respectively ($P < 0.05$).

**Table 1**

| Mortality rate | Retrospective group | Prospective group | *P* value |
|---|---|---|---|
| At first 24 hours | 28% | 7.6% | 0.04 |
| At day 7 | 80% | 26.9% | 0.001 |
| At day 30 | 82.8% | 53.8% | 0.01 |

**Conclusion** Using the presented treatment protocol for septic shock positively influenced mortality rate in the prospective group.

## P224

## A validation of different prognostic scoring systems in the prediction of outcome in peritonitis

**D Borisov, M Kirov, V Kuzkov, D Uvarov, E Nedashkovsky**
*Northern State Medical University, Arkhangelsk, Russia*
*Critical Care* 2005, **9(Suppl 1):**P224 (DOI 10.1186/cc3287)

**Background and goal** Early classification of patients with peritonitis by means of scoring systems provides adequate selection for surgical and therapeutic procedures and comparison of different therapies [1]. We compared the prognostic value of APACHE II and SAPS II scoring systems as well as the Mannheim Peritonitis Index (MPI) for assessment of outcome in the patients with diffuse bacterial peritonitis.
**Materials and methods** We enrolled 194 adult patients (mean age 49.6 ± 19.5 years) with secondary diffuse bacterial peritonitis in a prospective observational study during the period from 1999 to 2003. All patients were hospitalized in the ICU of the university hospital. The scores according to APACHE II, SAPS II, and MPI were assessed during 24 hours after admission to the ICU. The predictive values of the scores were estimated using regression analysis (coefficient of determination $r^2$). The discrimination was assessed using areas under the receiver operating characteristic curves (AUCs). Standardized mortality ratios (SMRs) were calculated. Variables were expressed as mean ± standard deviation or 95% confidence interval and as relative frequencies.
**Results and discussions** The mean APACHE II, SAPS II and MPI scores were 9.6 ± 8.4, 28.8 ± 16.7, and 23.9 ± 6.9, respectively. The hospital mortality rate was 19.1% (37 patients). The predicted mortality risk was 18.9%, 9.6%, and 33.6% for APACHE II (diagnostic category weight for gastrointestinal perforation/obstruction), SAPS II and MPI, respectively. The values of calibration ($P < 0.05$) and discrimination and SMR are summarized in Table 1.

**Table 1**

| | $r^2$/residual standard deviation | AUC/95% confidence interval | SMR |
|---|---|---|---|
| APACHE II | 0.87/12.1 | 0.87/0.82–0.92 | 1.01 |
| SAPS II | 0.89/11.7 | 0.82/0.76–0.87 | 1.99 |
| MPI | 0.38/24.3 | 0.85/0.79–0.90 | 0.57 |

The calibration was adequate for APACHE II and SAPS II scores. The discrimination was good for all systems. The APACHE II score had the most accurate overall mortality prediction, as reflected by the SMR.
**Conclusion** In patients with diffuse bacterial peritonitis, APACHE II is the most accurate prognostic scoring system as compared with SAPS II and MPI.
**Reference**
1. Bosscha K, van Vroonhoven ThJMV, van der Werken Ch: *Br J Surg* 1999, **86:**1371-1377.

## P225

## APACHE III outcome prediction after esophagectomy

**M Keegan, A Jacob, S Cassivi, F Whalen, D Brown, T Roy, B Afessa**
*Mayo Clinic College of Medicine, Rochester, MN, USA*
*Critical Care* 2005, **9(Suppl 1):**P225 (DOI 10.1186/cc3288)

**Introduction** The Acute Physiology and Chronic Health Evaluation (APACHE) III prognostic system has not been validated in patients admitted to the ICU after esophagectomy.
**Hypothesis** APACHE III predicts hospital mortality after esophagectomy.
**Methods** A retrospective review of all adult patients admitted to a single thoracic ICU after esophagectomy between October 1994 and December 2003. Patient demographics, ICU admission day APACHE III score, actual and predicted hospital mortality and length of hospital and ICU stays were collected for the first ICU admission only. Performance of the APACHE III prognostic system was assessed by the Hosmer–Lemeshow statistic for calibration and the area under the receiver operating characteristic curve (AUC) for discrimination.
**Results** There were 924 esophagectomies performed during the study period. Data are presented for the 483 patients that were admitted to the ICU. Mean age was 63.9 years. Mean APACHE III score on the day of ICU admission was 41.5 (standard deviation 18.1). Mean predicted (standard deviation) ICU and hospital mortality rates were 3.01% (6.31) and 7.90% (11.0), respectively. Median (interquartile range) lengths of ICU and hospital stay were 1.68 (0.79–3.79) and 13.52 (12.0–21.0) days, respectively. Observed ICU and hospital mortality rates were 2.7% (13 of 483 patients) and 5.4% (26 of 483), respectively.
There were differences ($P < 0.001$) between survivors to hospital discharge and non-survivors in age, acute physiology score and APACHE III score. Predicted ICU and hospital survival rates on the day of ICU admission were also different when survivors were compared with non-survivors ($P < 0.001$). Although most patients were male (82.6%), gender did not predict survival. The mean

(95% confidence interval [CI]) ICU and hospital length of stay ratios (observed/predicted) were 0.88 (0.76–1.00) and 1.01 (0.92–1.10), respectively.
The standardized ICU and hospital mortality ratios (95% CI), based on APACHE III prediction, were 0.89 (0.41–1.38) and 0.68 (0.42–0.94), respectively. In predicting mortality, the AUC of APACHE III prediction was 0.860 (95% CI 0.791–0.928) and the Hosmer–Lemeshow statistic was 8.581 with a *P* value of 0.379.
**Conclusions** The APACHE III prognostic scoring system has good discrimination and calibration in predicting hospital mortality of patients admitted to the ICU following esophagectomy. The low number of deaths may have influenced the statistical analyses.

## P226

### Multimodal strategies to improve APACHE II score documentation

**L Donahoe[1], M Kho[1], E McDonald[1], M Maclennan[2], S McIntyre[2], P Varga[2], D Cook[1]**
*[1]McMaster University, Hamilton, Canada; [2]St Joseph's Healthcare, Hamilton, Canada*
*Critical Care* 2005, **9(Suppl 1):**P226 (DOI 10.1186/cc3289)

**Background** The APACHE II score is used widely in the ICU setting. In our phase I study [1], APACHE II scores collected by an expert research coordinator and two research clerks were reliable (intraclass correlation coefficient = 0.90, lower 95% confidence interval [L-95% CI] = 0.85). However, we found substantial variability in the Chronic Health Index (CHI) (0.67, L-95% CI = 0.53) and Glasgow Coma Scale, verbal component (GCS-V) (0.42, L-95% CI = 0.25). To improve the reliability of the APACHE II score, we conducted phase II, aimed at changing the behaviour of ICU clinicians who are involved in documenting the APACHE II score in practice.
**Objective** To educate ICU clinicians regarding two specific components of the APACHE II score with suboptimal reliability: CHI and GCS-V.
**Design** An educational quality improvement interventional project.
**Population** ICU clinicians, primarily bedside nurses.
**Methods** We convened a combined clinical and administrative working group. In-person meetings, conference calls, and electronic communication were used to generate ideas for strategies that would efficiently serve our objective.
**Results** We implemented multimodal strategies to try to improve ICU clinicians' knowledge of, and compliance with, documentation of CHI and GCS-V. Strategies were: re-structuring the Clinical Information System Carevue (Philips, Andover, MA, USA), in-service education, use of local opinion leaders, reminders, audit and feedback, and support from the ICU Working Group (MDs, Allied Health professionals, bedside RNs, RN manager, RN educator, RN informatician [RNI]) who approved an improved CHI policy. We reconfigured the Carevue workstation screens to improve the visibility of CHI. In-services were conducted by an ICU educator and RNI. Education focused on the CHI components, GCS-V domain in intubated patients, and expectations for documentation of these items. As local opinion leaders, RNs (manager and charge nurses) prompted bedside nurses to complete chronic health documentation for all new admissions. We provided written information sheets, electronic resources, and computer-generated electronic reminders at RN workstations and on Carevue. The RNI provided regular, informal audit and feedback to bedside RNs to reinforce timely documentation.
**Conclusions** These diverse methods were delivered over 1 year, were multiply redundant to maximize the chance of behaviour change, were led by an integrated team of clinical and administrative managers, and were well accepted. We will next proceed to phase III, a formal re-evaluation of the reliability of the APACHE II score in our institution.
**Reference**
1. *Crit Care Med* 2004, **31(suppl):**A68.

## P227

### Comparison of Acute Physiology and Chronic Health Evaluation (APACHE II) and Simplified Acute Physiology Score (SAPS II) in a Greek general intensive care unit

**K Gkolfinopoulou, G Kouvatseas, A Armaganidis, U Dafni**
*National and Kapodistrian University of Athens, Greece*
*Critical Care* 2005, **9(Suppl 1):**P227 (DOI 10.1186/cc3290)

**Objectives** To determine the applicability of the Acute Physiology and Chronic Health Evaluation (APACHE II) scoring system, as well as that of the Simplified Acute Physiology Score (SAPS II) in an interdisciplinary intensive care unit in Greece and to evaluate the scores' ability to predict hospital mortality.
**Design** A prospective cohort study.
**Setting** A mixed medical and surgical intensive care unit at a major general hospital in the Athens Metropolitan area, Greece.
**Patients** A total of 309 adult patients, admitted to the ICU from January 2001 to January 2002, were enrolled in the study.
**Methods and results** Data enabling the calculation of APACHE II and SAPS II were collected for every patient on the day of admission. Patients' vital status at hospital's discharge was recorded. Probabilities of hospital death for patients were estimated by applying APACHE II and SAPS II, and predicted risks of hospital death were compared with observed outcomes. The patients' median age was 57 years old. The median APACHE II score was 15, higher in the 105 female patients (16) than in the 204 male patients (15). The median APACHE II estimated probability of death was 0.16 (0.2 for female patients and 0.14 for male patients). The median APACHE II was lower in the 168 operative cases (14) than in the 141 medical ones (16). The median APACHE II estimated probability of death was respectively 0.13 and 0.20 for the two groups. The median SAPS II score was 37 (40 for females and 36 for males, 35 for operative patients and 41 for medical patients). The median SAPS II estimated probability of death was 0.2 (0.25 for females and 0.18 for males, 0.17 for operative cases and 0.27 for medical cases). The overall goodness of fit and the areas under the receiver operating characteristic curve were assessed for the two scores.

## P228

### The impact of missing components of the Acute Physiology Score on the standardized mortality ratio calculated by the APACHE III prognostic model

**B Afessa, M Keegan, O Gajic, R Hubmayr, S Peters**
*Mayo Clinic College of Medicine, Rochester, MN, USA*
*Critical Care* 2005, **9(Suppl 1):**P228 (DOI 10.1186/cc3291)

**Introduction** In the APACHE III prognostic model, a weight of zero is given to missing and normal Acute Physiology Score (APS) values. The standardized mortality ratio (SMR) is used to evaluate the performance of an ICU. The objective of this study was to determine the impact of missing APS values on SMR.
**Methods** The study involved a retrospective analysis of the prospectively collected APACHE III database. The study population included adults treated in four intensive care units of a tertiary medical center with the APACHE III database. We obtained the APACHE III predicted mortality rate and hospital outcome. We

noted whether the first day values of the variables used to calculate the APS were missing. We created eight categories based on the number of missing values. We summarized descriptive data as mean (standard deviation [SD]), median (interquartile range [IQR]) and percentage. We created a logistic regression model to determine the association of the number of missing values with hospital mortality by entering the number of missing APS variables and the APACHE III predicted mortality rate as predictor variables. $P < 0.05$ was considered significant.

**Results** We had 49,682 admissions during the study period. Excluding patients who did not authorize their medical records to be reviewed for research and those with four or less available laboratory values, 42,607 patients were included in the study. Patients' mean (SD) age was 62.7 (17.3) years; 40,417 (94.9%) were white and 24,294 (57.0%) were male. The overall predicted and observed hospital mortality rates were 9.7% (4151/42607) and 12.0%, respectively, with SMR (95% confidence interval [CI]) of 0.813 (0.789–0.838). The median (IQR) predicted hospital mortality rate was 4.36 (1.65–13.20)%. Complete data were available in 934 (2.2%) admissions. The predicted mean and observed mortality rates as well as the SMR with the 95% CI for each of the missing categories are presented in Table 1. Four or more missing APS values were independently associated with higher observed hospital mortality.

**Table 1**

| Missing | Observed dead | Predicted dead | SMR (95%CI) |
|---|---|---|---|
| Zero | 183/934 (19.6%) | 25.8% | 0.76 (0.65–0.88) |
| One | 565/3607 (15.7%) | 19.6% | 0.80 (0.73–0.87) |
| Two | 952/9486 (10.0%) | 13.7% | 0.73 (0.69–0.78) |
| Three | 978/11641 (8.4%) | 10.4% | 0.81 (0.76–0.86) |
| Four | 753/8717 (8,6%) | 9.8% | 0.88 (0.82–0.95) |
| Five | 579/6799 (8.5%) | 9.5% | 0.90 (0.82–0.97) |
| Six | 127/1338 (9.5%) | 10.1% | 0.94 (0.79–1.12) |
| Seven or eight | 14/85 (16.5%) | 8.9% | 1.85 (1.01–3.11) |

**Conclusions** The majority of patients admitted to the ICU have one or more missing laboratory values needed to calculate the APS scores of the APACHE III prognostic system. When using such prognostic systems to evaluate the performance of ICUs, the number of missing values should be taken into consideration.

## P229

## Preliminary update of the Mortality Probability Model (MPM0)

**T Higgins[1], D Teres[2], W Copes[3], B Nathanson[4], M Stark[3], A Kramer[3]**

*[1]Baystate Medical Center, Springfield, MA, USA; [2]Tufts University, Boston, MA, USA; [3]Cerner Corporation, Kansas City, MO, USA; [4]OptiStatim, Longmeadow, MA, USA*

*Critical Care* 2005, **9(Suppl 1):**P229 (DOI 10.1186/cc3292)

**Introduction** The Mortality Probability Model (MPM II), developed on an international sample of 12,610 patients in 1989–1990, is used by Project IMPACT as a benchmarking tool. We updated the model based on more recent (2001–2004) data.

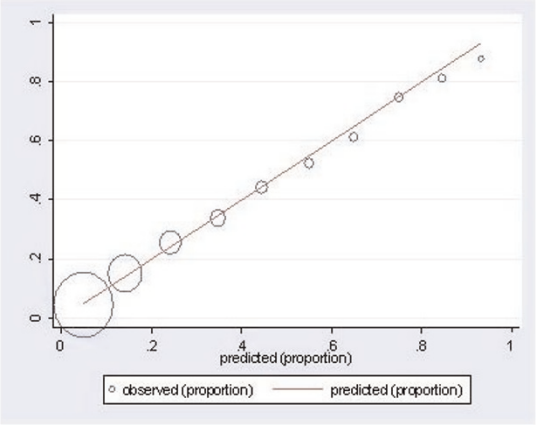
**Hypothesis and methods** Project IMPACT data on 125,610 patients age >18 and eligible for MPM scoring were analyzed. Multivariate analysis defined the relationship between hospital mortality and standard MPM physiologic variables plus patient type, location and lead time prior to ICU admission. The sample was randomly split into development and validation sets. Discrimination was assessed by ROC C statistic and calibration by graphic display and Hosmer–Lemeshow goodness of fit.

**Results** Overall mortality was 13.8%. The logistic model for all patients is presented in Table 1, and goodness of fit in Fig. 1. The area under the ROC curve was 0.82. Lead time and location did not influence outcome. Addition of a 'zero-factor' term for patients with no risk factors other than age improved model performance. Subgroup models (medical, coronary, trauma, neurosurgical, elective and emergent non-neuro, non-cardiac and non-trauma surgery) exhibit improved discrimination and calibration compared with the main model, which is superior in calibration to the existing MPM model.

**Table 1**

| Variable | Odds ratio | Coefficients | *P* value |
|---|---|---|---|
| Coma-stupor | 5.37 | 1.680172 | 0.000 |
| HR ≥ 150 | 1.77 | 0.570394 | 0.000 |
| SBP < 90 | 2.49 | 0.9111615 | 0.000 |
| Chronic renal | 1.68 | 0.5179099 | 0.000 |
| Cirrhosis | 2.18 | 0.7804761 | 0.000 |
| Metastasis | 2.69 | 0.9889827 | 0.000 |
| Acute renal | 2.17 | 0.7752536 | 0.000 |
| Arrythmia | 1.08 | 0.0782759 | 0.000 |
| Cerebrovascular | 1.31 | 0.2679498 | 0.000 |
| GI bleed | 0.84 | −0.1712258 | 0.003 |
| IC mass | 2.16 | 0.768795 | 0.000 |
| Age | 1.03 | 0.0302588 | 0.000 |
| CPR w/in 24 hours | 2.20 | 0.7888974 | 0.000 |
| Mechanical ventilation | 2.25 | 0.8123237 | 0.000 |
| Med/unsched S | 2.40 | 0.8760618 | 0.000 |
| Zero factors | 0.79 | −0.2368908 | 0.007 |
| Full code | 0.46 | −0.7693753 | 0.000 |
| Constant | NA | −4.778739 | 0.000 |

**Figure 1 (abstract P229)**




**Conclusions** Severity-adjusted mortality has decreased over time. Use of the updated model will allow more accurate assessment of quality of care. Subgroup models further improve discrimination and calibration and offer additional information in ICUs where the case mix is unusual.

**P230**

## Mortality prediction by hormonal profile versus APACHE score assessment in critically ill patients

**K Osman Hassan, S El-Maraghy, S El-Gengehy, D Ragab, K Abd El-Aziz, S Aref, H Mowafi, H Nagi**
*Cairo University, Egypt*
*Critical Care* 2005, **9(Suppl 1):**P230 (DOI 10.1186/cc3293)

**Objectives** To investigate hormonal changes during the acute phase of critical illness, to analyze their relationship to severity, and to evaluate their discriminating ability on critically ill patients' outcome.
**Design** A prospective cohort study of patients requiring intensive care.
**Setting** Adult medical, surgical and coronary care units in Mansoura University Emergency Hospital.
**Patients** A total of 40 consecutive patients requiring intensive care over a 5-month period and 10 healthy subjects of matched age and sex were selected as references control subjects.
**Interventions** For each patient included in our study the following was done. First, APACHE III score. Second, blood samples were taken in three occasions, on admission, third and seventh days of admission to the ICU. The plasma was separated and kept at −80°C until time of analysis. The following hormones (cortisol, growth hormone, thyroxin, and triiodothyronine hormones) were determined by ELISA technique.
**Measurements and main results** The best discriminators of patient outcome in descending order were the serum basal cortisol, then APACHE III score, then thyroxine hormone, then triiodothyronine on day 1 of admission with odd ratios of 11, 8.5, 3.2 and 2.85, respectively.
**Conclusion** Certain endocrinal parameters, mainly basal serum cortisol level obtained during ICU admission, might be simple, cheap and superior discriminators of patient outcome than the APACHE III score.

**P231**

## Serial evaluation of the Sequential Organ Failure Assessment score in non-coronary medical patients

**M Wehler, U Reulbach, E Hahn, R Strauss**
*University of Erlangen–Nuremberg, Erlangen, Germany*
*Critical Care* 2005, **9(Suppl 1):**P231 (DOI 10.1186/cc3294)

**Introduction** To determine the usefulness of daily Sequential Organ Failure Assessment (SOFA) score [1] for prediction of mortality in non-coronary medical ICU patients.
**Patients and methods** A prospective, observational study was conducted from May 1997 to April 2001. Nine hundred and nineteen consecutive adult patients admitted to the ICU for more than 24 hours were included (10,164 patient days). The SOFA score was calculated on admission and every 24 hours until discharge.
**Results** Study patients had a mean age of 59 ± 17 (± standard deviation) years; 70% were male, mean ICU length of stay was 11 ± 15 days, mean APACHE II score after 24 hours was 19 ± 10. Initial, maximum and mean (sum of daily SOFA scores divided through days of ICU stay) SOFA scores correlated well with mortality in the ICU (25.7%). The ability of the SOFA to discriminate between ICU survivors and non-survivors was assessed using the area under the receiver operating characteristic curve (AUC). The AUC was largest for the mean SOFA score (0.90, 95% confidence interval: 0.88–0.93) and the maximum SOFA score (0.88, 95% confidence interval: 0.86–0.91). A mean SOFA score of more than 7 corresponded to a mortality of more than 83% versus 10% for a mean score of 7 or less. When analyzing trends in the first 48 hours, regardless of the initial score, the mortality was 56% when the score increased, 24% when it remained unchanged, and less than 20% when it decreased.
**Conclusion** Sequential assessment of organ dysfunction during the first few days of ICU admission is a good indicator of prognosis. Both the mean and the maximum SOFA scores are particularly useful predictors of ICU outcome. Independent of the initial score, an increase in SOFA score during the first 48 hours predicted in our sample a mortality rate of 56%.
**Reference**
1. Vincent JL, *et al.*: *Intensive Care Med* 1996, **22:**707-710.

**P232**

## Association of the SOFA score and mortality in elderly patients with severe sepsis and septic shock

**R Machado[1], C David[1], G Oliveira[2], P Godoy[2], R Nagato[2]**
*[1]Universidade Federale, Rio De Janeiro, Brazil; [2]Prontocor, Rio De Janeiro, Brazil*
*Critical Care* 2005, **9(Suppl 1):**P232 (DOI 10.1186/cc3295)

**Introduction** The SOFA score is an excellent predictive marker of outcome in sepsis; however, there are very few studies that relate it to mortality in elderly patients with sepsis and septic shock.
**Objective** To assess the association of the SOFA score and other factors related to mortality in elderly patients with severe sepsis and septic shock.
**Methods** A 3-month prospective cohort study of 30 patients aged ≥ 65 showing severe sepsis or septic shock (Consensus Conference of 1991). Arterial hypotension (systolic arterial pressure < 90 mmHg) corresponded to the 'time-zero' of the study. The variables used were: SOFA score on days 1, 3, 5, 7, 14, and 28, ΔSOFA (variation of the SOFA score on days 1 and 3), APACHE II, Troponin I dosage, BNP and RCP, plasma glucose levels, organ failures [1], the presence of previous cardiovascular disease, assessment of dependence and cognitive deficit [2,3], length of ICU stay, and need for mechanical ventilation. We used Student's *t* test and the Fischer Exact test for a statistical analysis. We considered the significance level of 5%.
**Results** The mean age of patients, of whom 60% were females, was 82 ± 9 years (minimum = 65, maximum = 99). The predominant diagnosis was septic shock in 67% of the cases, while 33% of the patients developed severe sepsis. On days 1, 3, 5, 7, 14, and 28, the SOFA score presented mean values of 7, 6, 4, 3, 2, and 2, respectively (minimum = 2 and maximum = 15), thus evidencing a significant relationship between the SOFA score on day 1 ($P = 0.0001$) and day 3 ($P = 0.001$), including ΔSOFA score ($P = 0.043$), and mortality. The number of failures was also associated with mortality when two or more organic failures ($P = 0.001$) were present. Age, gender, APACHE II, length of ICU stay, dependence level, presence of cognitive deficit and/or previous cardiovascular diseases, plasma glucose levels, troponin I, BNP and RCP were not associated with the mortality.
**Conclusion** Mean SOFA average above 5 as well as SOFA variation within the first 72 hours proved to be good predictive markers in elderly patients with septic shock and severe sepsis. The same occurred in the presence of two or more organic failures during the course of sepsis.
**References**
1. Le Gall JR, Brun-Buisson C, Trunet P, Laturnerie J, Chantereau S, Rapin M: **Influence of age, previous health status, and severity of acute illness on outcome from intensive care.** *Crit Care*

*Med* 1982, **10:**575-577.
2. Katz S, Ford AB, Moskowitz RW: **Studies of illness in the aged: the index of ADL; a standardized measure of biological and psychosocial function.** *JAMA* 1963, **185:**914-919.
3. Lawton MP, Brody EM: **Assessment of older people: self-maintaining and instrumental activities of daily living.** *Gerontologist* 1969, **9:**179-186.

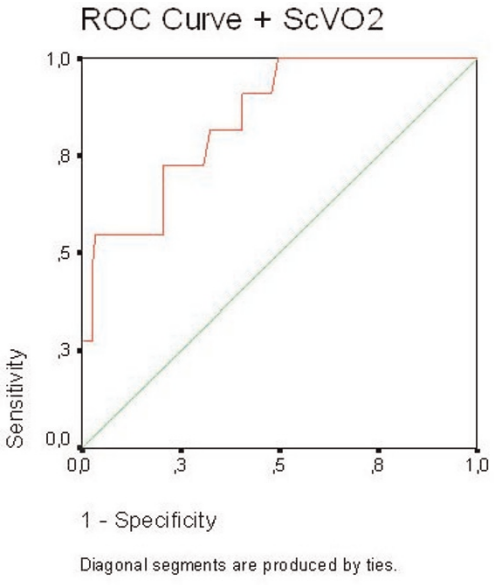
## P233

### Improvement of SOFA's predictive power for death when associated with central venous oxygen saturation intermittently obtained in the first 24 hours of cardiac surgery postoperation

**R Gomes, L Campos, P Nogueira, M Fernades, A Rouge, B Tura, BG Neto, C Rutherford, NW Gomes, HR Dohmann**
*Pró-Cardíaco, Rio de Janeiro, Brazil*
*Critical Care* 2005, **9(Suppl 1):**P233 (DOI 10.1186/cc3296)

**Background** Central venous oxygen saturation ($ScVO_2$) as well as SOFA, have been considered important parameters for follow-up, prognostic estimate, and therapeutic target in the management of critically ill patients.
**Objective** To analyze the impact of $ScVO_2$ on the postoperative (PO) period of cardiac surgery (CS), for the inhospital mortality predictive power of SOFA.
**Methods** A cohort of 132 consecutive patients selected from January 2004 to August 2004 and divided into the following two groups: GI, death ($n$ = 11, 8.3%); and GII, survivors. Blood samples were collected through a central venous catheter properly positioned in the right atrium. The $ScVO_2$ measurements were taken in the postoperative period as follows: immediately (SV0), after 6 hours (SV1), after 24 hours (SV2), and identified the lower $ScVO_2$ in each patient at the first 24 hours PO (SVL). SOFA was also registered on the first day PO. Inhospital mortality was considered when death occurred at any time during hospitalization. The $t$ test was used for statistical analysis, followed by six logistic regression (LR), classification tables and ROC curves.

**Figure 1 (abstract P233)**




**Results** Considering the total of the sample amount (132 patients), the mean SOFA was 4.03 ± 2.35 considering a GI value of 5.72 ± 3 and a GII value of 3.8 ± 2.2 ($P = 0.012$). $ScVO_2$ mean values and the $t$ test results of GI compared with those of GII were as follows, respectively: SV0 54.8 ± 12.6% vs 65.4 ± 8.9% ($P < 0.0001$), SV1 56.6 ± 7.3% vs 68.5 ± 5.9% ($P < 0.001$), SV2 61.1 ± 7% vs 69.3 ± 5.3% ($P < 0.001$) and SVL 50 ± 10% vs 62.7 ± 7.6% ($P < 0.001$). After the LR and the classification table have predicted a 50% mortality, the isolated SOFA score obtained a 91.7% accuracy (AUCROC 0.683, $P = 0.045$, confidence interval 0.499–0.867). From all the tested variables in LR with the SOFA score, the one that obtained a greater accuracy was SV2 (93.9%, AUCROC 0.846, $P < 0.001$, confidence interval 0.737–0.954) with sensibility of 73% and specificity of 79% with a likelihood ratio (+) 3.52 and (–) 0.34.
**Conclusions** The association between SOFA and $ScVO_2$ collected at the 24th hour of PO creates a prognostic model with better accuracy for predicting death at the first day of CS PO.

## P234

### Analysis of risk and prognostic factors of mortality in post-transplant patients in the intensive care unit

**S Cozzi, A Martini, N Menestrina, S Gazzani, V Schweiger, L Gottin**
*Policlinico GB Rossi, Verona, Italy*
*Critical Care* 2005, **9(Suppl 1):**P234 (DOI 10.1186/cc3297)

**Objective** To assess mortality's predictive factors in a cohort of bone marrow transplanted (BMT) patients admitted to the ICU.
**Design** A retrospective study.
**Setting** A 12-bed medico-surgical ICU.
**Patients** Twenty-nine patients on a total of 430 BMT (7%) from 1986 and 2004 were admitted to the ICU. Median age was 43 years and 22 patients were male (76%). Three main groups of underlying disease were found: three patients had acute myeloid leukaemia, 16 had acute myeloid leukaemia following myelodysplasia, 10 had lymphoproliferative diseases, 25 patients were neutropenic (86%), and 23 had less than 20,000 platelets/ml at admission to the ICU (79%). Nine had autologous transplant (2.7% of all autologous) and 20 allogenic transplants (20.4% of all allogenic). Numbers of supportive devices (such as mechanical ventilation or haemodialysis) were taken into account.
The SOFA score was calculated every day in the ICU (SOFA 0 at admission) and data were collected to calculate SOFA in the two days preceding ICU admission (SOFA –1 and SOFA –2). Main diagnoses at ICU admission were categorized as: acute respiratory failure without infection (ARF) and sepsis-related ARF (SD) that include severe sepsis and septic shock. Multivariate analysis with a logistic regression was used to analyze relationship between mortality and data regarding characteristics of patients, data regarding modality of transplant and cause of ICU admission. Univariate analysis was used to compare SOFA scores between groups.
**Main results** ICU admission occurred 23 days after transplant (median value), causes of ICU admission were: ARF (10%), SD (83%), others (7%). Overall ICU mortality was 90%. Relationship with mortality was found for allogenic versus autologous ($P = 0.04$), neutropenic versus non-neutropenic ($P = 0.03$), cause of ICU admission (SD vs ARF, $P = 0.026$).
The highest SOFA value, mean SOFA value, SOFA –2, SOFA –1.0 and SOFA +1 were higher in patients who died in ICU. No association was found between SOFA variation (differences from SOFA –1 and SOFA +1 and, respectively, SOFA 0 and SOFA +1). No relationship was found between mortality and number of

supportive devices, presence of severe thrombocytopenia, and underlying disease.

**Conclusions** Our data support previously known risk factors for ICU mortality in BMT recipients. SOFA was confirmed to well describe organ failure and predict mortality. No cutoff value was found to be highly suggestive for bad prognosis. Non-neutropenic autologous BMT recipients admitted to the ICU for non-sepsis-related acute pathologic event has a relatively good prognosis.

### P235

### Outcome of patients with systematic lupus erythematosus in the intensive care unit

**A Alzeer, A Al-Arfaj**
*King Khalid University Hospital, Riyadh, Saudi Arabia*
*Critical Care* 2005, **9(Suppl 1):**P235 (DOI 10.1186/cc3298)

The objective of the study was to identify the causes, outcome and prognosis of severe illness in patients with systematic lupus erythematosus (SLE) requiring ICU care in a university hospital over a 5-year period. The design was a cohort study. Forty-eight SLE patients requiring ICU management over a 5-year period (January 1997–December 2001) were studied prospectively. Of 48 patients, 14 (29.2%) died, predominantly with multiorgan dysfunction syndrome (MODS). Patients whose APACHE II score was $\geq 20$ had higher mortality than those with APACHE score $< 20$ (60% vs 7.1%; $P < 0.01$). All 18 patients whose health status was rated as 'good' survived, while 46.7% of 30 patients whose health was rated as 'poor' died ($P < 0.01$). Patients who had thrombocytopenia associated with sepsis and/or disseminated intravascular coagulopathy had the highest mortality (75%, 5-year survival). In conclusion, SLE patients admitted to the ICU had a lower mortality rate than some of the previous reports. Patients with SLE with high APACHE score $> 20$, poor health status, thrombocythopenia and MODS had poor prognosis in the ICU.

### P236

### The outcome and follow-up of trauma in elderly intensive care unit patients

**A Katsaros, V Gougoutas, S Karatzas, G Bartzis, P Athanasiou, V Zidianakis, P Myrianthefs, I Pastos, G Baltopoulos**
*'KAT' Hospital, Athens, Greece*
*Critical Care* 2005, **9(Suppl 1):**P236 (DOI 10.1186/cc3299)

**Introduction** Geriatric trauma is steadily expanded, mainly as a result of increased vehicle accidents. The outcome of geriatric trauma is considered significantly worse in comparison with that of younger people. Although the cutoff of age above which a patient is grouped as a geriatric one on a pathophysiological basis is not clear, patients above 65 years old are generally accepted as belonging to the geriatric group. In Greece, trauma is a very common disease and elderly patients are affected in a continuously increased manner. In our retrospective study we have recorded the incidence, ICU, hospital and home mortality as well as an approach to the quality of life of geriatric trauma critically ill patients after a period up to 5 years after ICU discharge.

**Methods** All multi-trauma patients over 65 years of age admitted in a seven-bed university ICU during the period 2000–2004 were recorded retrospectively. The collected data include: ICU mortality, hospital mortality, home mortality, and gross estimation of quality of life, 1–58 months after ICU discharge. For this estimation we used a simplified questionnaire on the basis of that published by Fernandez and colleagues [1], and the modified criteria are presented in Table 1. Each of them had the answer 'yes = 1 or no = 0' and the range can be between 0 and 10. The information for the outcome of patients outside the hospital was taken by telephone communication of ICU physicians with the patients or their relatives.

**Table 1**

| |
|---|
| Dressing |
| Psychology |
| Total |
| Patient |
| At home? |
| Oral communication |
| Urination control |
| Defecation control |
| Food adequacy |
| Personal cleaning |
| Home movement |
| Outside movement |

**Results** During a nearly 5-year period (lasting from 2 March 2000 to 14 November 2004) 229 multi-trauma patients were admitted to our seven-bed university ICU. Seventy of them (31%) were above 65 years old (mean ± standard error, 76.5 ± 8). Thirty-seven (53%) (77 ± 9 years old) died inside the ICU. The remaining 33 (76.5 ± 6.6 years, range 66–89) were discharged from the ICU and treated on different medical departments (surgical, neurosurgical, etc.). Seven of them died during the hospital stay outside the ICU. The outcome 1–58 months after ICU discharge was recorded after telephone communication in 15 from the remaining 26 patients. From those 15 patients, three died at home and 12 (17% of the total 70 patients) are alive 32.6 ± 9.6 months after discharge. Nearly all the alive stay at home and they have an excellent quality of life on the basis of our simplified scale (with the exception of one patient the mean value is 9.3 ± 1).

**Conclusions** Geriatric trauma has a poor prognosis with high ICU mortality. In our study the ICU mortality of geriatric multi-trauma patients was in accordance with the literature [2]. The follow-up of these patients is difficult, at least on a retrospective basis, and in our study we have obtained data from about two-thirds of the whole number of hospital discharged patients. Surprisingly, the quality of life in this restricted part of geriatric patients can be characterized as very good or excellent.

**Reference**

1. Fernandez RR, *et al.*: **Validation of a quality of life questionnaire for critically ill patients.** *Intensive Care Med* 1996, **22:**1034-1042.
2. Jacobs D: **Special considerations in geriatric injury.** *Curr Opin Crit Care* 2003, **9:**535-539.

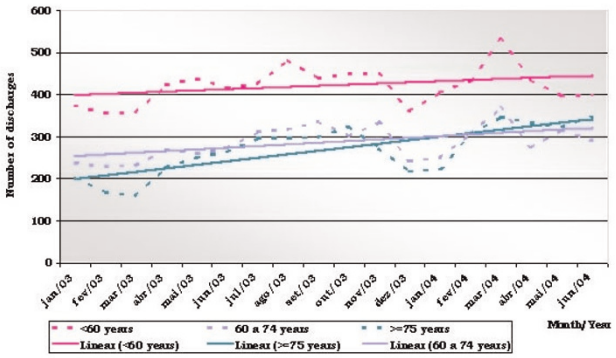
### P237

### Trends of age utilization in intensive care unit resources are matched by the population aging process in Brazil

**M Rocha, D Schout, A Santoro, S Oliveira, M Knibel**
*Comite QuaTI – AMIB/DIXTAL, Sao Paulo, Brazil*
*Critical Care* 2005, **9(Suppl 1):**P237 (DOI 10.1186/cc3300)

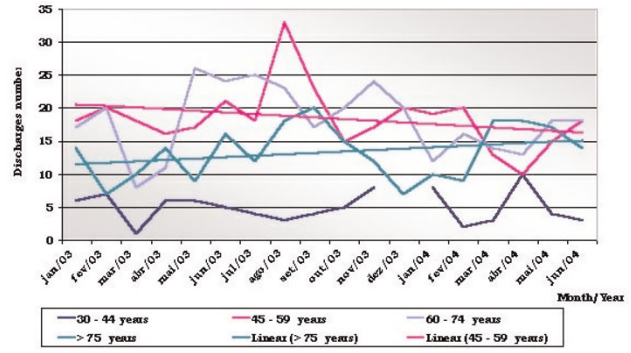
**Introduction** The QuaTI System, sponsored by AMIB and DIXTAL, is developing an important database for intensive care in Brazil. The QuaTI System offers significant information for the participating ICUs for their continuous improvement, and gives data, although partial, of demographic characteristics of patients seen at participant ICUs. In our country, there is a steady decline in

**Figure 1 (abstract P237)**




Monthly distribution of hospital discharges by age group: QuaTI System, January 2003–June 2004.

**Figure 2 (abstract P237)**




Distribution discharge diagnosis: acute myocardial infarction by age group, QuaTI System, January 2003–June 2004.

natality and mortality in the past 30 years, showing an irreversible and accelerated aging population process. Life expectancy at birth is 68 years and expectation at 60 years is more 18 years on average. In 1970, 5.07% of the population was older than 60; in 2000, 8.56%; and in 2002, 9.3%. In the South and Southeast, 10.2% of population are more than 60 years old.

**Materials and methods** The QuaTI System is formed by 54 ICUs. Descriptive analysis of the database for the period January 2003–June 2004.

**Results and discussion** The database contains 17,620 records. We observed a linear growing tendency for all age groups. In the 60–74 years old age group there is a more marked increase in relation to those younger than 60 years old. Patients older than 75 years show an even more accentuated tendency, as shown in Fig. 1. The conditions responsible for this increase are acute myocardial infarction (Fig. 2) and femur fracture. In this database, 58.8% of all records are of patients older than 60 years, 28.7% between 60 and 74 years old, and 30.1% older than 75 years. These findings confirm the trends shown by populational studies in Brazil and call the attention of ICU care providers to develop plans to support this older group of patients with proper care.

## P238

## Hospital mortality associated with day and time of discharge from intensive care units in the United Kingdom

**S Harvey, H Wunsch, C Welch, D Harrison, K Rowan**
*ICNARC, London, UK*
*Critical Care* 2005, **9(Suppl 1):**P238 (DOI 10.1186/cc3301)

**Background** The day and time of admission to the ICU does not affect subsequent hospital mortality in the United Kingdom after adjustment for severity of illness [1]. An independent editorial published alongside this study [2], commented that "time and day of discharge from the ICU may have an even greater impact on patient outcomes" because of reduced staffing levels and services on the wards at weekends and at night.

**Aim** To investigate whether day or time of discharge is associated with subsequent hospital mortality.

**Design** A retrospective cohort study.

**Setting** One hundred and seventy-two adult general (medical/surgical) ICUs in England, Wales and Northern Ireland participating in the Case Mix Programme.

**Population** A total of 174,361 consecutive admissions between December 1995 and June 2004 discharged alive from the ICU to a ward in the same hospital (not for palliative care).

**Analysis** The day of the week, defined *a priori*, commenced at 08:00 hours on one day to 07:59 hours the following day. Each weekday was spilt into three time periods: day 08:00–17:59 hours; evening 18:00–23:59 hours; and night 00:00–07:59 hours. Crude and case mix adjusted hospital mortality were calculated for the day of the week and the time of day of discharge from the ICU.

**Results** After exclusions for APACHE II, 144,210 admissions to 172 ICUs were included in the analysis. Most patients were discharged during the day ($n$ = 113,595, 79%) compared with evening ($n$ = 26,345, 18%) and night ($n$ = 4270, 3%). Discharges were lowest on Sunday ($n$ = 13,638) and highest on Friday ($n$ = 25,069). Selecting Wednesday (day of week) and day (time of day) as reference, discharge on Sunday or Monday was associated with higher crude hospital mortality compared with Wednesday (Sunday odds ratio [OR] 1.12, 95% confidence interval [CI] 1.04–1.20; Monday OR 1.19, 95% CI 1.11–1.26). These were no longer significant after adjusting for case mix (Sunday OR 1.04, 95% CI 0.96–1.13; Monday OR 1.02, 95% CI 0.96–1.09). Discharge in the evening and at night was associated with higher crude hospital mortality compared with day (evening OR 1.37, 95% CI 1.32–1.43; night OR 1.47 95% CI 1.34–1.61), which was still significant after adjusting for case mix (evening OR 1.22, 95% CI 1.16–1.28; night OR 1.34, 95% CI 1.20–1.50).

**Conclusion** Hospital mortality is not associated with day of the week of discharge from the ICU but is associated with time of day of discharge. As previously reported, this is partly due to premature discharges from the ICU occurring more frequently in the evening and/or at night [3], but may also be due to discharged patients not receiving the appropriate level/amount of care on the wards at these times, possibly due to reduced staffing levels. Further investigation is warranted.

**References**

1. Wunsch, *et al.*: **Hospital mortality associated with day and time of admission to intensive care units.** *Intensive Care Med* 2004, **30:**895-901.
2. Bell CM, Scales DC: **Variation in intensive care unit outcomes by day of week: no weak-end.** *Intensive Care Med* 2004, **30:**739-734.
3. Goldfrad C, Rowan K: **Consequences of discharges from intensive care at night.** *Lancet* 2000, **355:**1138-1142.

**P239**

## Health-related quality of life and functional performance predictors in secondary peritonitis patients

**K Boer, C Mahler, B Opmeer, O van Till, J Reitsma, M Boermeester, C De Borgie**
*Academic Medical Center, Amsterdam, The Netherlands*
*Critical Care* 2005, **9(Suppl 1):**P239 (DOI 10.1186/cc3302)

**Introduction** Health-related quality of life (HR-QoL) is an important patient outcome, playing a complementary role to both mortality and long-term morbidity outcomes in the assessment and measurement of treatment effects and hospital process. Our aim is to determine predictive factors for the HR-QoL in patients with secondary peritonitis. We evaluated patient, surgery and postoperative characteristics to determine their roles in HR-QoL.
**Methods** Patients participating in an ongoing trial evaluating surgical strategies for secondary peritonitis were consecutively surveyed by questionnaire 6 months after initial laparotomy. Eighty-three patients were asked to fill in the Euroqol-5 Dimensions (EQ-5D) and Euroqol Visual analogue scale (VAS) measuring HR-QoL, while their attending doctors assessed the Karnofsky performance scale, measuring functional impairment, at the outpatients clinic.
**Statistical analysis** Univariate analysis was carried out using the Mann–Whitney U test, the Kruskal–Wallis analysis of ranks and the Wilcoxon rank test. Relationship significance was determined by the Spearman's rank correlation coefficient. Multivariate analyses were done by general linear model main effects model, using patient characteristics, disease characteristics and postoperative characteristics.
**Results** The following factors were determined predictive in the univariate analysis and were therefore added to the multivariate analyses: age, gender, enterostomy, comorbidity (assessed by the Charlson index), type of contamination, and finally length of hospital stay (LOH) (LOH was used as a summary value to represent, length of ICU stay, ventilation duration, and the number of relaparotomies; as these were all highly correlated). Predictive factors for worse HR-QoL measured by the VAS, determining overall patient well-being, are: being female ($\beta = -11.1$, $P = 0.009$); having an enterostomy ($\beta = -8.8$ $P = 0.049$); purulent contamination ($\beta = -11.0$, $P = 0.028$); LOH stay ($\beta = -14.5$, $P = 0.042$); and severity of comorbidity ($\beta = -3.6$, $P = 0.063$). Predictive factors for poor mobility are: increasing age ($P = 0.030$); being female ($P = 0.026$); having an enterostomy ($P = 0.014$); and LOH stay ($P = 0.019$). Predictive factors for reduced ability to care for oneself are: having an enterostomy ($P = 0.031$); and LOH stay ($P = 0.003$). Predictive factors for limited ability to perform daily activities are: having an enterostomy ($P = 0.011$); LOH stay ($P = 0.037$); and severity of comorbidity ($P = 0.018$). Only being female ($P = 0.060$) was predictive for reporting more pain. Predictive factors for increased depression and anxiety are: being younger ($P = 0.005$); purulent contamination ($P = 0.010$); and faecal contamination ($P = 0.003$). LOH stay was the only predictive factor for the Karnofsky performance scale ($\beta = -25.2$, $P < 0.001$).
**Conclusion** Six months following initial surgery, it appears that LOH stay and enterostomy are overall the most predictive factors for HR-Qol and functional impairment in patients with secondary peritonitis.

**P240**

## Quality of life 6 months after discharge from an intensive care unit

**D Markantonaki, C Nikolaou, M Lascou, N Magina**
*Agia Olga, Athens, Greece*
*Critical Care* 2005, **9(Suppl 1):**P240 (DOI 10.1186/cc3303)

**Objective** The objective of this study is to determine the quality of life of patients 6 months after their discharge from the ICU and its relationship to age, the APACHE II score during admission, admitting diagnosis, and length of stay.
**Design** One hundred and forty-five consecutive patients were admitted to the ICU from August 2001 to June 2003 and that fulfilled the following criteria: age >18 years, an ICU stay longer than 4 days, and place of residence Greece.
Of the 145 patients, 47 died within 6 months of their discharge from the ICU, and from the rest 38 (20 men, 18 women) completed the questionnaire and were included in the study.
**Methods** After telephone contact and briefing, a special questionnaire was sent by post. The questionnaire was completed by the patient, or if he/she was unable to by his/her relative or the closest person that was living with him/her. The questionnaire that was used was the Short Form Survey 36. This questionnaire has a very good reliability and validity and has been weighted for the Greek language. It consists of 36 questions in eight health dimensions that yield summary measures in two higher order clusters of mental and physical health. Data analysis was performed using the non-parametric Kruskal–Wallis test.
**Results** The average age of the participating patients was 56.71 years, the average APACHE II score at admission was $14.84 \pm 7.23$ and the average length of stay was 15.84 days. Every health dimension was scored separately and received a value from 0% to 100%. The lowest average score that was recorded was 31% and concerned the physical role scale, while the highest average score was 76% and concerned the bodily pain scale. In the rest of the scales the scores ranged from 44% to 59%. In a model that compared quality of life scores for each dimension separately, with age, with APACHE II scores at admission, with length of stay and with admitting diagnosis to the ICU, statistical significance was observed between age and physical functioning ($P = 0.015$), vitality ($P = 0.024$) and social functioning ($P = 0.014$).
**Conclusions** Limitations were noted in the physical role, that is the parameter that evaluates social well-being, return to work and participation in daily activities. Age was the only variable that seemed to be related to physical functioning, that is the ability to perform physical activities, social functioning, that is participating in social activities, and vitality, the subjective feeling of tiredness and exhaustion.

**P241**

## Changes in health-related quality of life in severe sepsis

**J Hofhuis[1], J Bakker[2], H van Stel[3], A Schrijvers[3], J Rommes[1], P Spronk[1]**
*[1]Gelre Ziekenhuizen Location Lukas, Apeldoorn, The Netherlands; [2]Erasmus MC, Rotterdam, The Netherlands; [3]Julius Centre University Medical Centre, Utrecht, The Netherlands*
*Critical Care* 2005, **9(Suppl 1):**P241 (DOI 10.1186/cc3304)

**Introduction** Mortality from severe sepsis remains high despite ongoing searches to improve treatment modalities. Patients may survive sepsis at the cost of an impaired health-related quality of life (HRQOL). We hypothesized that HRQOL decreases during

severe sepsis and intensive care (IC) treatment and remains impaired several months after IC survival and discharge.

**Methods** We performed a long-term prospective study in patients with severe sepsis admitted to a 10-bed mixed IC unit in a 654-bed university-affiliated hospital. Patients were included if they met predefined criteria of severe sepsis and were admitted to the IC unit for > 48 hours. A population of sex-matched and age-matched healthy Dutch individuals served as control. The HRQOL was assessed using the Short-form 36 (SF-36), a generic instrument for measuring health status in different domains (i.e. physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health). Patients or proxies completed this questionnaire in the first 48 hours of admission [1]. Patients with established sepsis completed the SF-36 at IC discharge, hospital discharge, and 3 and 6 months after IC discharge. Demographic data and admission severity of illness (APACHE II score) were obtained. Statistical comparisons at admission and at 6 months were done with *t* tests, changes over time were assessed with both univariate and multivariate analysis of variance.

**Results** Of the 170 patients with severe sepsis 95 could be evaluated 6 months after IC discharge (eight patients were lost to follow-up, 67 patients had died). In all dimensions of the SF-36, HRQOL changed significantly over time in survivors of severe sepsis ($P < 0.05$). These changes over time were not influenced by age or admission APACHE II score. A distinct pattern of a sharp decline during IC treatment and gradual improvement approaching normal functioning at 6 months after IC discharge was found in almost all HRQOL dimensions (i.e. physical functioning, role-limitation due to physical, vitality, general health, emotional role, social functioning, and mental health). Nevertheless, the average SF-36 scores of survivors of severe sepsis were still lower in six of the eight dimensions 6 months after IC discharge with the exception of social functioning and bodily pain compared with a normal population (all $P < 0.05$). Interestingly, the pre-admission HRQOL of severe sepsis survivors was already lower in three of the eight dimensions (role-physical, mental health and vitality) when compared with HRQOL in the normal population (all $P < 0.01$).

**Conclusion** In survivors of severe sepsis, HRQOL showed a sharp multidimensional decline during IC treatment and gradual improvement approaching normal values 6 months after IC discharge. Pre-admission HRQOL was already lower in severe sepsis survivors than in the normal population. This interesting finding in view of the risk of surviving sepsis warrants further research.

**Reference**

1. Hofhuis J, Hautvast JLA, Schrijvers AJP, Bakker J: **Quality of life on admission to the intensive care: can we query the relatives?** *Intensive Care Med* 2003, **29:**974-979.

## P242

### Stress, anxiety and depression in cardial infarct and bypass surgery patients

**J Grailet[1], S Deckers[2], V Fraipont[1], A Etienne[2], F Damas[1]**
*[1]CHR Citadelle, Liège, Belgium; [2]ULg, Liège, Belgium*
*Critical Care* 2005, **9(Suppl 1):**P242 (DOI 10.1186/cc3305)

**Introduction** Our study aimed at studying stress, anxiety and depression symptoms of ICU patients while focusing on a restricted pathology (i.e. patients with cardiac disease), and while comparing the impact of stress between patients exposed to different levels of medical information (i.e. informed bypass surgery patients versus uninformed inaugural infarct patients) and to a different perceived control of their medical treatment (i.e. controlled uncomplicated stay vs uncontrolled complicated stay).

**Materials and methods** Thirty-two ICU patients not older than 75 were assigned to either one of four subgroups according to their medical history: complicated bypass (CB), uncomplicated bypass (UB), complicated infarct (CI) and uncomplicated infarct (UI). All patients were examined twice. On Time 1 (2 days after discharge from ICU) they answered stress (Perceived Stress Scale [PSS]) and post-traumatic stress questionnaires (the Impact of Events Scale [IES]), the Hospital Anxiety and Depression Scale (HADS) and the State subscale of the State-Trait Anxiety Inventory (STAI-T, testing constitutive anxiety). On Time 2 (6 weeks later), they answered the same scales minus the STAI-T. Assuming that bypass patients are better informed than infarct patients, and the fewer the complications the larger the sense of control, we tested the hypothesis that CI patients would performed badly on our scales whereas UB would do better.

**Results** On Time 1, overall results indicated poor levels of stress, anxiety or depression. Yet UI patients steadily produced the lowest scores of the sample, whereas bypass patients produced the highest. UI patients thus presented less depressive symptoms on the HADS ($H = 8.335$, $P = 0.039$). The STAI-T results also showed a dissociation between those patients who experienced complications (CI and CB) and those who did not (UI and UB): self-rated 'anxious' patients were more numerous in the 'complicated' groups CI and CB ($F = 4.614$ and $P = 0.005$).

On Time 2, measures of stress remained low on the PSS. Yet signs of post-traumatic stress (IES) emerged in bypass patients (CB and UB) and to a lesser extent in CI patients, with significant group effects in the avoidance scale ($F = 2.286$ and $P = 0.036$) and in the total scale ($F = 3.13$ and $P = 0.042$) of the IES.

**Conclusion** Our results show mild signs of stress, anxiety or depression shortly after release of ICU. Yet some consistent post-traumatic stress affects bypass patients several weeks later. UI patients steadily display the weakest symptoms of all. In contrast to our initial hypothesis, 'informed' bypass patients presented the strongest signs of stress, anxiety and depression, while the 'control' factor primarily impacts on infarct patients.

## P243

### Prevalence of symptoms related to post-traumatic stress disorder during long-term follow-up in patients after surgical treatment for secondary peritonitis

**C Mahler, K Boer, C Unlu, M Vroom, B Lamme, D Gouma, C de Borgie, M Boermeester**
*Academic Medical Center, Amsterdam, The Netherlands*
*Critical Care* 2005, **9(Suppl 1):**P243 (DOI 10.1186/cc3306)

**Background** Symptoms related to post-traumatic stress disorder (PTSD) may occur after exposure to a traumatic event and are clustered; symptoms of re-experiencing, symptoms of avoidance, and hyperarousal symptoms. It is unknown to what extent recovered peritonitis patients experience PTSD-related symptoms. The aim of this study was to screen patients for persisting PTSD-related symptoms 4–10 years after surgical treatment for secondary peritonitis and to detect whether a difference is observed in prevalence of PTSD-related symptoms in patients with ICU admission and those without.

**Methods** An existing database of 278 patients surgically treated for secondary peritonitis between 1994 and 2000 revealed that by October 2003, 131 patients were alive of which 118 patients could be tracked. A standardized validated questionnaire was mailed. PTSD-related symptoms were measured by the Post-Traumatic Stress Syndrome 10-Questions Inventory (PTSS-10) and the Impact of Events Scale Revised questionnaire (IES-R). PTSS-10 scores > 35 or IES-R scores > 39 were regarded as

fitting with PTSD-related symptoms. In addition, information regarding the presence of traumatic memories was obtained.
**Results** The response rate was 88%; 101 questionnaires were suitable for analysis (86%). The mean age of the responders was 58.3 (± 14.5) years and 59% was male. The mean follow-up period after peritonitis was 7.2 (4.0–10.4) years. The mean APACHE II score on admission and Mannheim Peritonitis Index score at operation were 9.5 (± 5.2) and 22.0 (± 7.4), respectively. Sixty percent of the patients had been admitted to the ICU for a mean of 19 (± 16) days. Overall PTSS-10 scores and IES-R scores were 25.4 ± 13.6 and 28.5 ± 31.7, respectively. According to the PTSS-10 questionnaire, the overall prevalence of PTSD-related symptoms was 23%. The symptoms were observed in 28% of former ICU patients and in 15% of non-ICU patients ($P = 0.21$). The IES-R revealed an overall prevalence of PTSD-related symptoms in 29% of patients, 31% of former ICU patients versus 25% of non-ICU patients ($P = 0.78$). The concordance rate between the questionnaires was 80%. Furthermore, the presence of a traumatic memory was significantly related to the scores on the PTSS-10 ($P = 0.03$) and on the IES-R ($P = 0.04$).
**Conclusion** Long-term follow-up of patients after admission for peritonitis showed a prevalence of symptoms fitting with PTSD in 23–29%. In peritonitis patients, attention should be given to early recognition of this presumably underestimated problem. Given the size and duration of the problem, research is needed into preventative measures.

### P244

### Initial assessment of a guesthouse for relatives of patients admitted to a general intensive care unit

**Y Goren, J Cohen, O Ben Shimon, S Raz, P Singer**
*Rabin Medical Center, Petah Tikva, Israel*
*Critical Care* 2005, **9(Suppl 1):**P244 (DOI 10.1186/cc3307)

**Introduction** The families of critically ill patients constantly worry about the welfare of their loved ones. To this end, we recently established a guesthouse in close proximity to our ICU exclusively serving the families of patients hospitalized in the unit. The purpose of this study was to evaluate their response to this new service.
**Methods** The ICU comprises a 10-bed acute care unit and a four-bed mechanical ventilation weaning unit. The guesthouse comprises six single rooms, a communal kitchen and bathing facilities, situated on the floor below the ICU. The guesthouse is restricted to use by relatives of ICU patients. All families are informed of this option at the first meeting with the ICU staff and rooms are allocated when available (i.e. no specific criteria for allocating a room are applied). Once a patient is no longer being treated in the ICU, the room must be vacated. Questionnaires were distributed to the first 80 families using the facility, after the occupant had vacated the guesthouse. Where appropriate, responses were graded on a scale of 1 (negative response) to 5 (very positive response).
**Results** The rate of return was 43/82 (52.4%). All the guests were first-degree relatives of the patients. Mean traveling time from home to the hospital was 1.26 hours (range, 0.25–3.5 hours). The mean duration of stay was 19.69 (range, 2–120) days, and 31/40 (77%) respondents to this question stayed in the guesthouse for the whole period. Two respondents used this service only on Saturdays when religious Jews do not drive, whereas the remainder used it intermittently. Forty guests (93.02%) gave as the main reason for requesting a room a strong need to remain at the hospital at all times. Thirty-eight (88.37%) felt that the continuous presence of one family member at the hospital enabled other family members to continue with their daily routine. The majority (55.81%) graded the physical conditions of the guesthouse as 5/5, 37.2% as 4/5 and 6.9% as 3/5. Regarding close contact with other families, 23.2% felt this to have a very positive impact, 18.6% a moderate impact, 34.1% felt it had no impact and 4.65% claimed this had a negative effect. There was a very positive response both to the way the ICU staff interacted with the guests (mean score 4.69) and to fulfilled expectations (mean score 4.41). Finally, 37% felt a similar service should be provided to all families in the hospital, 30% only in selected cases, and 30% only to families of ICU patients.
**Conclusion** The positive feedback received is encouraging and suggests that a definite need has been fulfilled. Efforts should be made to open such facilities in other units in the hospital, especially ICUs.

### P245

### Re-humanization in the intensive care unit: perspective of the staff

**P Souza, M Lugarinho, A Santana, M Guianze, S Silva, L Félix**
*Hospital de Clinicas Niterói e Mário Lioni, Rio de Janeiro, Brazil*
*Critical Care* 2005, **9(Suppl 1):**P245 (DOI 10.1186/cc3308)

**Objectives** Humanization was introduced in our ICU in 1996. We performed research with patients and relatives, but never audited the staff's opinion. Through research for the ICU staff (doctors, nurses, respiratory therapists), we tried to create a profile of their point of view and then to improve the re-humanization program.
**Materials and methods** Between January and March 2004, we carried out research with 15 questions about our re-humanization program, the profile of the interviewer and comments. The data were analyzed and communicated by posters inside the ICU. Our sample was 52 questionnaires.
**Results** The answer rate was 96.5%. The mean age was 28.7 years old, 64.3% were female, 51.8% Catholics, and between 10 months and 5 years of labour time in the ICU. The idea and the program of re-humanization is important for 95.4%, but around 50% did not know it in detail. Noise was a problem in 67.3%. Relatives disturbed nurse's work for 82.6%. For patients, stress factors were fear (57.7%), anxiety (53.9%) and solitude (55.8%)
**Conclusion** Listening to the staff, we could improve re-humanization and approximate who is involved. The staff has to understand the importance of the process and be aware of benefits from taking care with dignity.

### P246

### Protecting healthcare workers from SARS

**C Gomersall, G Joynt, P Lam, T Li, F Yap**
*The Chinese University of Hong Kong, Shatin, Hong Kong*
*Critical Care* 2005, **9(Suppl 1):**P246 (DOI 10.1186/cc3309)

**Introduction** There are only limited data from which to estimate the risk to ICU healthcare workers of acquiring SARS. We describe our experience of infection of healthcare workers in our SARS ICU.
**Methods** The study was a retrospective audit of the outcome of measures to prevent SARS infection among ICU staff. During the study period (13 March–31 May) only patients with SARS or suspected to have SARS were admitted to our ICU. Data extraction was carried out by a trained research nurse. The following data were collected: patient demographic data, duration of invasive mechanical ventilation, place of intubation, ICU length of stay, number of days with diarrhea and days from symptom onset to ICU admission. Duration of exposure to SARS patients was obtained from nursing and medical rosters. Infection control

procedures evolved during the first few weeks of the epidemic. In brief, the final protocol consisted of the following. All staff entering the ICU were required to clean their hands and don a gown, gloves, hat, face shield and fit-tested N95 or N100 mask. Initial fit-testing involved a qualitative fit-test, with a subsequent quantitative test for those who failed the qualitative test. Those staff for whom an adequate fit could not be achieved with a N95 or N100 mask were issued with powered air purifying respirators.

**Results** Sixty-seven patients with SARS were admitted, with eight patients being admitted twice. The median (interquartile range [IQR]) length of ICU stay was 13 (6–24) days. The mean (standard deviation) number of days between symptom onset and ICU admission was 9.5 (4.7) days. The median (IQR) age was 47 (36–59) years and median (IQR) APACHE II score 10 (8–13). Thirty-two patients were ventilated for a median (IQR) of 14.5 (7–25) days. Total number of ventilated patient-days was 525 days. No patients received non-invasive ventilation. All patients who were ventilated were intubated by ICU doctors, 28 in the ICU and four in other areas of the hospital. Diarrhoea occurred in 55% of patients. Thirty-five doctors worked in the ICU for a median (IQR) of 284 (97–376) hours. One hundred and fifty-two nurses and healthcare assistants worked for a median (IQR) of 119 (57–166) hours. Five ICU healthcare workers developed SARS (2.67%, 95% confidence intervals 1.15–6.11). Four of these were nurses and the fourth was a healthcare assistant. Three became symptomatic in the first 10 days of exposure to patients with SARS, strongly suggesting that they were infected in the first few days of exposure. Three of the five were subsequently underwent quantitative fit-testing of the N95 mask that they were using at the time of infection. In all cases the fit was adequate.

**Conclusion** The incidence of SARS among healthcare workers in our ICU was low despite a prolonged period of exposure to patients with SARS. Three of five infections occurred when the protective strategies were being developed and vigilance in the correct use of protective equipment was probably lowest.

## P247

## Burnout syndrome among intensive care staff

**M Cubrilo-Turek**
*Sveti Duh General Hospital, Zagreb, Croatia*
*Critical Care* 2005, **9(Suppl 1):**P247 (DOI 10.1186/cc3310)

**Background** Burnout is a syndrome of emotional exhaustion (EE), depersonalization (DEP) and lack of personal accomplishment (PA). The Maslach Burnout Inventory (MBI) is a widely used psychometric instrument for measuring excessive job-related stress in different working areas.

**Objective** To determine the existence of the burnout syndrome among medical (MICU) and surgical (SICU) intensive care staff.

**Methods** A sample group of 41 nurses and emergency physicians from the MICU and 30 from the SICU was tested anonymously by MBI using a 22-item questionnaire. Statistical analyses were carried out by X ± standard deviation, and Mann–Whitney rank sum *t* test ($P < 0.05$).

**Results** Total scores (X ± standard deviation) of the MBI were higher for the MICU (65.53 ± 6.78) than for the SICU (55.7 ± 3.89) staff ($P < 0.05$). MICU staff showed a moderate degree of EE (24.97 ± 11.25), DEP (6.06 ± 5.64), and PA (34.44 ± 8.85). The same parameters showed better results among the SICU staff; a low degree of EE (17.10 ± 5.27), as well as a low level of MBI DEP (5.27 ± 5.08), and a moderate degree of PA (33.70 ± 9.85). Between the groups statistically significant differences were found for total MBI and EE ($P < 0.05$). There were no significant differences between MICU and SICU staff for DEP or PA parameters. Overall job burnout was represented in a moderate degree.

**Conclusion** Early recognition of burnout as a result of prolonged stress and frustration among intensive care staff contributes to better professional behaviour, organizational structure changes in the work environment and better health care quality for critically ill patients.

## P248

## The use of a checklist to guide multidisciplinary rounds improves the utilization of prophylactic and safety actions in a closed intensive care unit

**S Silva, G Schettino, R Conish**
*Sirio Libanes, São Paulo, Brazil*
*Critical Care* 2005, **9(Suppl 1):**P248 (DOI 10.1186/cc3311)

**Background** Checklist forms have been successfully used during multidisciplinary rounds in an 'open' ICU to increase the use of prophylactic and risk reduction interventions.

**Objective** To evaluate the benefits of using a checklist form in a 'closed' ICU to increase the utilization of prophylactic and safety interventions.

**Methods** The data of the head of bed position, peak inspiratory pressure during mechanical ventilation, deep vein thrombosis and digestive bleeding prophylaxis were recorded for 2 weeks before ($n = 93$ cases) and after ($n = 72$) the implementation of a checklist (modified from [1]) to guide the multidisciplinary visit in the morning, noon, and night in a high-complexity (22 medical/surgical beds) 'closed' ICU.

**Results** The percentage of patients with head bed position > 30° (49% vs 77%, $P < 0.001$) and the use of deep vein thrombosis prophylaxis (61% vs 82%, $P < 0.001$) increased after the use of the checklist during the rounds. Digestive bleeding prophylaxis (93%) and limiting the peak inspiratory pressure $< 35\ cmH_2O$ (90%) were observed in almost all patients in the pre-checklist period and this intervention did not increase their utilization (94% vs 90%, respectively, $P = 0.6$).

**Conclusion** As previously demonstrated in 'open' ICUs, using a checklist to guide the multidisciplinary rounds is helpful to increase the utilization of prophylactic and safety interventions in a 'closed' ICU.

**Reference**

1. Pronovost P, Berenholtz S, Dorman T, Lipsett P, Simmonds T, Haraden C: **Improving communication in the ICU using daily goals.** *J Crit Care* 2003, **18:**71-75.

## P249

## The monitoring of vital signs on adult medical wards

**C Brown, K Daly, R Beale**
*Guy's & St Thomas' NHS Foundation Trust, London, UK*
*Critical Care* 2005, **9(Suppl 1):**P249 (DOI 10.1186/cc3312)

**Aims** Ward patients have been found to have abnormal vital signs in the hours prior to ICU admission and preceding cardio-pulmonary arrest. This study aimed to assess nursing staffs' knowledge of vital signs, and whether they increase the frequency of observations in response to abnormal values.

**Method** The study was performed over a 24-hour period on the medical wards of a London hospital. Observations charts of 233 patients were audited; 634 sets of observations were documented. Accepted normal values for this study were; temperature 36.0–37.4°C; heart rate 50–99 beats/min; systolic BP 100–179 mmHg; respiratory rate 10–19 breaths/min; $SaO_2$

**Table 1 (abstract P249)**

| | Normal range (A) | > normal range (B) | < normal range (C) | A vs B | A vs C |
|---|---|---|---|---|---|
| Temperature | 6.43 (5.89–6.97) | 3.47 (2.64–4.31) | 5.20 (4.05–6.35) | 0.000 | 0.238 |
| Heart rate | 6.28 (5.78–6.78) | 3.62 (2.70–4.55) | 3.06 (0.61–6.74) | 0.000 | 0.056 |
| Blood pressure | 5.79 (5.33–6.26) | 5.37 (3.09–7.66) | 3.63 (2.57–4.69) | 0.710 | 0.126 |
| Respiratory rate | 6.29 (5.14–7.45) | 5.76 (5.08–6.44) | None recorded | 0.380 | |
| Oxygen saturation | 6.15 (5.61–6.71) | Invalid category | 4.79 (3.97–5.61) | | 0.000 |

≥ 95%. Comparisons were made of the time interval between observations when values were both within and outside the defined range. To assess the knowledge of nursing staff, questionnaires were given to 101 staff; 73 were returned (72% response). The questionnaire had questions about normal values for vital signs and the significance of deviation from these norms.

**Results** Comparisons of the intervals between observations are presented in Table 1. Data are given as the mean interval in hours with 95% confidence intervals. A Mann–Whitney U test showed a significant difference in frequency of observations for increased heart rate, increased temperature and decreased $SaO_2$. No significant difference was detected for abnormal respiratory rate or BP. Performance on the questionnaire was poor; 56% of respondents obtained less than 50%. Areas of concern were oxygen therapy (12%), hypotension (15%), respiratory assessment (23%), recognition of oliguria (31%) and normal respiratory rate (49%).

**Conclusion** Ward staff failed to increase the frequency of observation for abnormal respiratory rate and BP. Performance in the questionnaire suggests that staff may not understand the clinical significance of these vital signs.

## P250

## Prehospital emergency medicine and non-heart-beating donors: is there a future together?

**A Lufinha[1,2], C Ferreira[2,3]**
*[1]Hospital Militar Principal, Lisbon, Portugal; [2]Hospital São Francisco Xavier SA, Lisbon, Portugal; [3]Hospital Curry Cabral, Lisbon, Portugal*
*Critical Care* 2005, **9(Suppl 1):**P250 (DOI 10.1186/cc3313)

**Objectives** One of the major questions for transplant coordination teams in Portugal is how to expand the donors' pool, in order to satisfy the population needs. The use of non-heart-beating donors (NHBD) could help to deal with this problem of organ shortage. In addition to difficulties with legal and ethical acceptability, there are concerns regarding medical safety, which prevent the widespread use of these donors [1].

**Methods** Lisbon has an emergency medical service with a response time under 10 min and all four Prehospital Emergency Medical Teams (VMER) are able to perform all kinds of advanced life support manoeuvres *in situ* and during transport to hospital. We perform a retrospective study of all cardiopulmonary arrest emergency calls (112 calls) assisted by our VMER, at Hospital S Francisco Xavier, during 2003. Then, we analyse how many of these cases could have 'matched' a protocol for uncontrolled NHBD [2]; that is, patients who die outside of hospital and are transported to hospital for organ donation.

**Results** In 2003, our VMER assisted 2266 emergency calls; 13.8% (312) were cardiopulmonary arrest (CPA) cases and advanced cardiac life support was always performed. All major trauma and drowning events, as well as patients older than 55 years of age, were excluded (total of 217) from this study. Only 16.9% (16) of the remaining CPA (95) were resuscitated (less than our global average rate of 27%) and transported to the hospital with return of spontaneous circulation. A total of 79 cases resulted in patients who died outside of hospital and could have been transported to the hospital for organ donation if there were a protocol for NHBD in Portugal.

**Conclusions** An average rate of 25% of all CPA events assisted by our VMER could have resulted in NHBD A specific protocol must be developed in the near future because non-heart beating programmes are a good option to increase the donors' pool. Current data suggest that organs and tissues obtained are of the same or better quality than those obtained from encephalic death donors [3].

**References**

1. Arias-Diaz J: **Non-heart-beating donation: current state of the art.** *Transplant Proc* 2004, **36:**1891-1893.
2. *Protocol of NHBD*. Madrid: Transplantation Care Unit, Hospital Clinic San Carlos.
3. Rio Gallegos F: **Non heart beating donors. Successfully expanding the donor's pool.** *Ann Transplant* 2004, **9:**19-20.

## P251

## Organ donation: a 10-year experience

**M Sharpe, R Butler, C Harris**
*London Health Sciences Centre – University Campus, London, Canada*
*Critical Care* 2005, **9(Suppl 1):**P251 (DOI 10.1186/cc3314)

**Introduction** There is a growing disparity between patients placed on a waiting list and those who are transplanted, and the number of patients who die while on a waiting list is also increasing. A 10-year retrospective chart review was performed on all organ donors to define our current practice in order to propose initiatives to increase our organ donor rate.

**Results** Seventy-seven charts were reviewed; mean age of donors was 47 ± 16 years (range 16–82). A vascular accident (77%) was the most common etiology of brain death. An organ donor management protocol had not been developed. The majority of patients (87%) had central venous pressure monitoring; only 21% patients had a pulmonary artery catheter. Complications included diabetes insipidus (DI) (74%), hypotension requiring inotropic/vasoconstrictor support (88%) and hypothermia (100%) requiring active warming measures; 9/10 patients who had no invasive pressure monitoring were receiving inotropic support. The majority of patients (47%) had an abnormal serum sodium with hypernatremia as the most common abnormality. The mean number of organs donated per donor was 3.29 ± 1.21; the kidney was the most utilized (87%), followed by the liver (73%), heart (44%), lung (18%), pancreas (8%) and intestine (1%). As the number of inotropic support medications increased, there was a tendency for the mean number of organs donated per donor to decrease ($P = 0.1$; Table 1).

**Conclusions** Without an organ donor management protocol, there was a considerable variation in the management of our organ

**Table 1 (abstract P251)**

| Number of agents | *n* | Number of organs tx/donor |
|---|---|---|
| 0 | 9 | 3.8 ± 1.3 |
| 1 | 32 | 3.7 ± 1.1 |
| 2 | 27 | 3.4 ± 1.3 |
| 3 | 8 | 3.3 ± 1.3 |
| 4 | 1 | 3 |

donors. Hypotension, DI and electrolyte disturbances were common complications and many patients required fluid resuscitation and inotropic support as well as pharmacological treatment for DI. With the institution of an organ donor management protocol that includes the administration of triple hormonal therapy (thyroxine, vasopressin, glucocorticoid), we have begun a prospective study to determine the impact of an organ donor management protocol on organ donor complication rate, the need for inotropic support and whether this will result in an increase of number of organs per donor transplanted.

## P252

### Availability of organs for transplantation: a 15-year overview on organ donation in the ULB network

**F Hut[1], I Senepart[2], L De Pauw[2]**
*[1]CUB-Hôpital Erasme, Brussels, Belgium; [2]CHU-Hôpital Brugmann, Brussels, Belgium*
*Critical Care* 2005, **9(Suppl 1):**P252 (DOI 10.1186/cc3315)

**Introduction** Transplantation of solid organs has become a widely performed and accepted procedure that is mainly restricted by the availability of organs. The gap between the supply of organs and the demand for transplantation is still increasing, resulting in longer waiting times and increased mortality for patients waiting for a transplant.
**Method** A retrospective analysis of donor and transplant data charts was conducted over a 15-year period in the ULB network.
**Results** From 1990 until now, 1070 potential donors were referred and 508 (47.4%) of them were used for transplantation. During the study period, the mean age of the donors increased from 35 to 48 years, the percentage of trauma as cause of cerebral death decreased from 42% to 20%, the retrieval rate for the abdominal organs (kidney, liver, pancreas) remained stable whereas for the hearts it dropped significantly.
**Conclusion** In the ULB network, despite a changing pattern in the organ donors' profile, the availablity of abdominal organs remains constant. The situation in heart donation is alarming.

## P253

### Estimated weight and height of critically ill patients: how reliable are these values in acutely admitted patients?

**R Determann, E Wolthuis, M Vroom, M Schultz**
*Academic Medical Center, Amsterdam, The Netherlands*
*Critical Care* 2005, **9(Suppl 1):**P253 (DOI 10.1186/cc3316)

**Introduction** Patients' weight (W) and height values (H) are often unknown on acute admittance to the ICU. In the present study we investigated: (a) whether estimated W&H are in agreement with W&H values given by patients/relatives, and estimated H is in agreement with measured H; and (b) whether body mass index (BMI) and H influence estimated W&H values.
**Methods** One hundred consecutive acutely admitted patients (from whom pre-admission W&H were unknown) were included. W&H were recorded from medical/nurse ICU records ('estimated W&H'). Afterwards, patients or close relatives were asked for pre-admission W&H ('actual W&H'). In addition, H was determined with a tape measure ('measured H'). Patients were divided into four BMI (calculated from actual W and measured H) groups and four height groups. The mean difference was calculated to assess bias between both methods. Ranges of 95% limits of agreement were calculated to assess agreement between both methods for individual patients. Statistics were by regression analysis.
**Results** (a) The mean difference (95% confidence interval) between actual and measured H was 0.9 (0.3–1.4) cm. The mean difference between estimated and measured H was 1.0 (−0.2 to 2.3) cm. The 95% limits of agreement were −4.6 to 6.4 cm and −10.1 to 12.2 cm, respectively. The mean difference between estimated and actual W was 1.8 (0.7–2.9) kg. The 95% limits of agreement were −9.3 to 12.9 kg. (b) See Table 1 for data of agreement between estimated and actual W for BMI subgroups. See Table 2 for data of agreement between estimated and measured H for height subgroups.

**Table 1**

| BMI group | < 20 (*n* = 12) | 20–24.9 (*n* = 35) | 25–29.9 (*n* = 39) | ≥30 (*n* = 14) |
|---|---|---|---|---|
| 95% limits of agreement | −7.2 to 15.1 cm | −10.6 to 11.8 cm | −6.9 to 10.7 cm | −13.0 to 18.4 cm |

**Table 2**

| Height group | <165 cm (*n* = 18) | 165–174 cm (*n* = 31) | 175–184 cm (*n* = 40) | ≥185 cm (*n* = 11) |
|---|---|---|---|---|
| 95% limits of agreement | −11.5 to 13.0 kg | −9.6 to 13.8 kg | −9.7 to 12.1 kg | −9.4 to 6.2 kg |

**Conclusions** Estimated W&H match actual W and measured H of acutely admitted ICU patients very well. W estimation is more variable for the highest BMI group.

## P254

### Quality in the intensive care unit: a general intensive care unit compared with a cardiointensive unit

**P Souza, V Souza, N Nunes, L Tavares, W Alcântra**
*Hospital de Clinicas Niterói e Mário Lioni, Rio de Janeiro, Brazil*
*Critical Care* 2005, **9(Suppl 1):**P254 (DOI 10.1186/cc3317)

**Objectives** Nowadays, to improve quality is not only a challenge, but a question of survival of an institution. There is no consensus how to study quality in ICU. The objective was to study the evolution of some variables that could improve outcome. The name of the system is QuaTI, a Brazilian small animal; the name remembers the word quality (qualidade, in Portuguese). We compared a general ICU with a cardiointensive unit (CIU).
**Materials and methods** The period of study was January–October 2004. We studied, on a monthly basis, the following variables: age, sex, length of stay in ICU (LOS), occupation rate (OR), real mortality rate, invasive mechanical ventilation rate, accidental extubation, pneumothorax by accidental punction and pressure ulcers and casemix. We compared the results of a general ICU with a cardiointensive ICU.
**Results** Our data are: age ICU = 60.6 years old vs CIU = 62.4 years old; sex ICU male = 53% vs CIU = 61.8%; LOS ICU = 5.3

vs CIU = 3.8; OR: ICU = 93% vs CIU = 96%; real mortality rate ICU = 14.5% vs CIU = 3,6%; invasive mechanical ventilation ICU = 25.6% vs CIU = 17.3%; accidental extubation ICU = 1.4% vs B (CIU) = 0.8%; pneumothorax by accidental punction HCN (ICU) = 2.8 vs CIU = 0; and pressure ulcers HCN (ICU) = 3.7% vs CIU = 0.5; the casemix in the ICU was 33.3% neurologic, 19.4% respiratory and 15.6% cardiovascular, and in the CIU the casemix was 77.2% cardiovascular, 8.5% neurologic and 5.1% respiratory.
**Conclusion** The study of the performance of one ICU is difficult, complex and expensive. The best way to know one specific performance is to compare it with similar ICUs that have similar resources and casemix. To compare a Brazilian ICU with a European or American ICU is not ideal and could give equivocal information that generates erroneous decisions. With QuaTI, we begin a very interesting project that will create a Brazilian databank on ICU performance.
In our study, the main difference is the casemix, with much more neurologic cases in the ICU versus the CIU where predominant is cardiovascular, 77.2%. The outcome of mortality is completely different – 14.5% versus 3.6%. Our worse rates as pressure ulcers could be explained by the casemix (more neurologic patients), and the difference among the pneumothorax is explained because in a CIU we usually do not make profound venous access. The main importance is to have data and establish strategies for improved quality and safety. The QuaTI works in this direction.

## P255

### Quality of care on an intensive care unit: using subjective indicators as an analysis tool

**M Knibel[1], C David[2], R Hatum[1]**
*[1]CardioTrauma Ipanema Hospital, Rio de Janeiro, Brazil; [2]Federal University of Rio de Janeiro, Brazil*
*Critical Care* 2005, **9(Suppl 1):**P255 (DOI 10.1186/cc3318)

**Introduction** The routine follow-up of objective quality indicators (product analysis) and subjective quality indicators (service analysis) has essential importance to adequate management of an ICU. It allows continuous PDCA cycles (to plan, to do, to check and to act) and the adoption of preventive and corrective measures, which is a simple, dynamic and efficient management system.
**Patients and methods** We applied satisfaction questionnaries to patients admitted from February to November 2003 and their relatives. These questionaries generated the Patient Satisfaction Index (PSI) and the Relative Satisfaction Index (RSI), by means of the 17 patients' answers and 10 relatives' answers. The statistical analysis used: Mann–Whitney test (to compare two groups in which variables did not present a normal distribution), Kruskal–Wallis analysis of variance (to compare three or more groups), chi-squared test (to compare qualitative data between each 5-month period), and Pearson coefficient (to measure the correlation strength between PSI and RSI). We accepted $P < 0.005$ as significance level. The software pack used was the SAS® system.
**Results** Indexes general descriptive analysis: PSI 2.856 (mean value), RSI 2.882 (mean value). PSI descriptive and statistical analysis by month: no difference ($P = 0.10$). RSI descriptive and statistical analysis by month: no difference ($P = 0.005$). PSI descriptive and statistical analysis by 5-month period: no difference ($P = 0.31$). RSI descriptive and statistical analysis by 5-month period: no difference ($P = 0.65$). Correlation coefficient between PSI and RSI: positive correlation ($P = 0.0001$ $r = 0.516$).
**Conclusions** Our management system was good in services issue because: (1) the PSI mean was 2.856 and the RSI was 2.882 – both above 2.5, our initial goal; (2) there was no significative variance in the PSI between the months, which indicates a uniform behavior of the service; (3) there was no significative difference in the PSI and RSI measures between both 5-month periods, which shows uniformity in the offered services; and (4) there was strong association between PSI and RSI, which confirms that the ICU team really sees patients' relatives like clients, which means a good quality of service.

## P256

### Managing performance in the intensive care unit: a new system in Brazil

**P Souza[1], J Lain[1], J Andrade[1], M Lugarinho[1], M Amaral[2], R Turon[1]**
*[1]Hospital de Clinicas Niterói e Mário Lioni, Rio de Janeiro, Brazil; [2]Hospital Evangélico, Rio de Janeiro, Brazil*
*Critical Care* 2005, **9(Suppl 1):**P256 (DOI 10.1186/cc3319)

**Objective** The study of the performance of one ICU is still setting up. There is no consensus about criteria to guarantee quality. To analyse the performance of an ICU and to benchmark it with other ICUs could be a valuable experience. The objective was to study the performance of one ICU and, for benchmarking proposes, to compare it with itself and against a standard composed of seven other ICUs. The name of this system is QuaTI, a Brazilian small animal; the name remembers the word quality (qualidade, in Portuguese).
**Materials and methods** A group of intensivists supported by a Brazilian producer of medical equipment (Dixtal) have created a computer program that collects many variables that compose the idea of performance.
We register, on a daily basis, variation of the data studied, the mean value, the mean value of benchmarking (the same subject in other ICUs), and control graphics (with upper limit and lower limit of control covering a confidence interval of 95%). This information is in one ICU computer covering a period of 16 weeks; every 3 months we receive a report with more complete analyses, and after 12 months there is a special report with consolidated information. The data are divided into management, clinical and risk indicators. Each group of indicators are composed of some data; for example, risk indicators are composed of the rate of patients with some infection, rate of accidental extubation, rate of pneumothorax by barotraumas, rate of pneumothorax by venous puncture, and rate of pressure ulcers. The system has confidentiality, so you only know your data and the benchmarking, but not the data from one specific ICU. The databank is the domain of AMIB (Brazilian Society of Intensive Medicine). We start using QuaTI at the end of 2001. There were 30 ICUs in the system at the end of 2002 and 56 at the end of 2003.
**Results** We could compare the performance of our ICU with ourselves along time, every 3 months, each year and with data from benchmark ICUs. With this information we know our comparative performance and we can decide whether it is necessary to change some processes on a real and comparative basis.
**Conclusion** The study of the performance of one ICU is difficult, complex and expensive. The better way to know one specific performance is to compare it with similar ICUs that have similar resources and casemix. To compare a Brazilian ICU with a European or American ICU is not ideal and could give equivocal information that generates erroneous decisions. With QuaTI, we begin a very interesting project that will create a Brazilian databank on ICU performance.

**P257**

## The value of daily routine chest radiographs in intensive care patients

**M Graat, E Wolthuis, G Choi, J Stoker, M Vroom, M Schultz**
*Academic Medical Center Amsterdam, The Netherlands*
*Critical Care* 2005, **9(Suppl 1):**P257 (DOI 10.1186/cc3320)

**Introduction** It is uncertain whether daily routine chest radiographs (CXRs) truly affect the daily management of critically ill patients. The consensus opinion of the American College of Radiology, however, is that routine CXRs are indicated in all mechanically ventilated patients (http://www.acr.org).
**Methods** The study was performed in a mixed surgical/medical ICU. During a period of 6 months, routine CXRs were performed next to CXRs on clinical indication (on-demand CXRs). During a second phase of 3.5 months, the routine CXR was abandoned and only on-demand CXRs were made. Questionnaires (on the back side of each CXR request form) were completed for all CXRs, addressing the indication and expected findings. The presence of the following abnormalities was scored by the radiologist: pulmonary abnormalities (atelectasis, major infiltrates, any pneumothorax, pulmonary congestion or significant pleural fluid), and abnormal position of any invasive device (tube, central venous lines). Statistical analysis was by chi-squared test.
**Results** During the first 6 months, 5180 CXRs were made in 888 patients (3400 routine and 1780 on-demand CXRs). Of all routine CXRs, only 221 revealed an unexpected abnormality (6.5%) compared with 249 of the on-demand CXRs (14.0%) ($\chi^2 = 79.42$, df = 1, $P < 0.0001$). These findings included (on the routine CXRs) 1.2% malposition of the tube, 1.1% malposition of central venous lines and 1.2% atelectasis, versus 1.8% malposition of the tube, 1.8% malposition of central venous lines and 1.2% atelectasis in the on-demand CXRs. In the second period, 1093 (all 'by definition' on-demand) CXRs were made in 425 patients. Of these CXRs, 153 revealed an 'unexpected' abnormality (14.3%) ($\chi^2 < 0.0001$, df = 1, $P$ = not significant); these findings included 2.2% malposition of the tube, 2.7% malposition in central venous lines and 2.8% pleural fluid.
**Conclusion** Compared with the first period, the number of on-demand CXRs did not change in the second period. In addition, the incidence and type of unexpected findings of on-demand CXRs did not change. From this we can conclude that daily routine CXRs may not be necessary for all ICU patients.

**P258**

## Accidental catheter removal in the intensive care unit: a prospective observational study

**S Myatra, J Divatia, P Mehta, S Kalaniya, R Sareen**
*Tata Memorial Hospital, Mumbai, India*
*Critical Care* 2005, **9(Suppl 1):**P258 (DOI 10.1186/cc3321)

**Introduction** Accidental catheter removal (ACR) is associated with complications caused by the removal itself and by catheter reinsertion. Hence determining the incidence is important to implement preventive measures. The objective of the present study was to analyse the incidence of ACR for all types of catheters in the ICU.
**Methods** A prospective observational study in a 22-bed medical/surgical ICU-HDU in a 550-bed tertiary cancer care center on all consecutive adult ICU patients between 1 October 2004 and 30 November 2004. ACR was considered to be accidental removal of a catheter either by the patient or by the ICU staff. The incidences of ACR for all types of catheters per 100 catheters (%) and per 100 catheter-days (%cds) were determined. Complications arising due to the ACR were noted. The nurse–patient ratio during the ACR and daily was noted.
**Results** A total of 913 catheters were inserted in 147 patients for a total of 3614 catheter-days. ACR occured in 43 catheters (4.7%, 1.19%cds) in 25 patients. The incidence of ACR was higher for arterial than for central venous catheters (2.4 vs 0.7%cds). The incidence of ACR for nonvascular catheters (%cds) was: endotracheal tube 1.65; nasogastric tube 2.9; urinary catheter 0.17; thoracic drain 0.56; abdominal drain 0.53; epidural catheters 1.1; and neck drains 0. Four patients (9.3%) with accidental ETT removal had transient arterial hypoxemia necessitating reintubation. Twenty-six catheters (60%) – six ETT, seven arterial, 10 nasogastric, one thoracic and two others – needed reinsertion. The daily median nurse–patient ratio was 0.36 (range 0.27–0.57), and during ACR it was 0.38 (0–1).
**Conclusion** Our incidence of ACR was high for nasogastric tubes, arterial lines and ETTs. Development and implementation of improved protocols are essential to reduce the incidence of ACR in these catheters. There was no obvious correlation between ACR and nurse–patient ratio. To minimize ACR, it is necessary to monitor its incidence carefully and to implement preventive measures.

**P259**

## Complications of care in a neonatal–paediatric intensive care: first results of a prospective observational survey

**V Payen, A Maury, K Norbert, E Saliba, S Cantagrel**
*Hopital Gatien de Clocheville, Tours, France*
*Critical Care* 2005, **9(Suppl 1):**P259 (DOI 10.1186/cc3322)

**Background** Adverse events can increase the mortality or morbidity of patients hospitalized in ICUs. Their frequency in paediatric or neonatal ICUs is between 8% and 45%. A survey of these complications is an indicator to improve quality of care.
**Objectives** To evaluate by a prospective observational survey over a 1-year period the frequency of iatrogenic complications in a multidisciplinary paediatric and neonatal intensive care unit; to examine their type, severity, associate factors that favour their occurrence, and the role of medical staff and parents in precipitation or detection of iatrogenic complications.
**Patients** All consecutive admissions of patients over a 1-year period from October 2004 to October 2005 in a paediatric and neonatal intensive care unit
**Preliminary results** After 1 month, 71 children were admitted, 53% in neonatal and 47% in paediatric ICUs. Seventy-five per cent of all admissions were for medical reasons, 20% after surgery and 5% following trauma. There were 42 iatrogenic complications in 31 patients (44% of admissions). Peripheral venous catheter complications represented the major adverse event (50%) with 81% of diffusion followed by skin oedema; respiratory events involved 24% of complications and included accidental extubations (69%) and laryngeal dyspnea (16%); bedsore were found in 18% of adverse events; 7% of them are secondary to the arterial or central venous catheter. Forty-six per cent were major, 7% were moderate and 47% were minor. No death was directly due to complications. Human error was implicated in 46% of cases; 46% of iatrogenic complications did not have any explanation. They were related mostly to insufficient surveillance. Precipitating staff members were nurses in 73% of times, especially for minor events. They detected the majority of the complications (81%).
**Conclusion** As in adult ICUs, iatrogenic complications are frequent in paediatric and neonatal ICUs. Knowledge of adverse events frequency is a precious source for quality improvement.

## P260

### Adverse events and death in patients with community-acquired pneumonia in the emergency department of a major university hospital in Brazil

**A Machado, R Gallotti, H Novaes, M Lorenzi, J Neto, I Velasco**
*Hospital das Clínicas, São Paulo, Brazil*
*Critical Care* 2005, **9(Suppl 1):**P260 (DOI 10.1186/cc3323)

**Introduction** Adverse events (AEs), defined as unintended injuries due to medical care, have been related to patient death. Urgent care is an important AE risk factor.
**Objectives** This paired case–control study aimed to identify the occurrence of AEs in patients with community-acquired pneumonia (CAP) attending a medical Emergency Department (ED) of a Brazilian major university hospital, disclosing the AEs categories associated with death.
**Methods** We investigated 202 patients admitted for CAP from March 1996 to September 1999. The cases comprised 101 consecutive deaths and the controls 101 discharged patients matched for primary diagnosis and admission period. AEs, detected by chart review, were classified regarding: severity degree (major and minor), immediate cause, and professional category. The association with death was analyzed by multivariate conditional regression including variables related to demographic features, severity on admission and care characteristics.
**Results** A total of 603 AEs were identified in 202 patients: 456 events (75.6%) in 85 cases and 147 (24.4%) in 55 controls. Two hundred and twenty-four major AEs were detected: 201 events in 65 cases and 23 in 10 controls. Diagnostic procedures and nursing activities accounted for 43.1% of all events. Nursing (43.8%) and medical (36.5%) AEs were the main professional categories of AEs detected in both groups. The occurrence of at least one AE was associated with a higher risk of death, with adjusted odds ratio (OR) estimates of 2.99 (95% confidence interval [CI] = 1.09–8.17; $P = 0.033$). A stronger association with death was found regarding major AEs (OR 6.05; 95% CI = 2.19–16.68; $P = 0.001$). Medical AEs and administrative AEs were also associated with death, with adjusted OR estimates of 3.74 (95% CI = 1.40–10.00; $P = 0.009$) and 2.97 (95% CI = 1.12–7.90; $P = 0.029$), respectively.
**Conclusions** In summary, AEs predominated among the deceased patients admitted with CAP. Diagnostic and therapeutic procedures and nursing activities corresponded to the main AE immediate causes. Regarding the professional involved, AEs related to nurses and physicians predominated. The occurrence of AEs was associated with a higher risk of death in CAP patients admitted to a tertiary ED.

## P261

### Adverse medication events in the intensive care unit: avoidable or inevitable?

**J Mitchell, F Cox, J Wagg, J Farrimond**
*Royal Brompton & Harefield NHS Trust, Harefield, UK*
*Critical Care* 2005, **9(Suppl 1):**P261 (DOI 10.1186/cc3324)

**Introduction** Recent publications have focused on patient safety and managing medications effectively [1]. Adverse reactions to medicines and medication errors cost the National Health Service (NHS) approximately £0.5 billion per annum [1]. To inform practice and facilitate policy revision we explored medication errors in two specialist cardiothoracic ICUs that utilise identical reporting mechanisms.
**Methods** A retrospective analysis of the DATIX risk management database was performed for the 3-year period January 2002–November 2004. These events were categorised using the National Patient Safety Agency impact and consequence classifications [2]. Events categorised as moderate or severe were individually investigated and an individual risk reduction strategy initiated.
**Results** During this 3-year period 114 medication-related adverse events were reported. There were 9.5 events per 1000 ICU bed-days. A toal 14.9% of events were categorised as moderate or severe, while 85.1% were insignificant or mild.

**Table 1**

| Event type (all) | Number (% of total) | Major events (%) |
|---|---|---|
| Prescribing | 20 (18) | 3 (3) |
| Supply | 11 (9) | 2 (2) |
| Mislabelling | 18 (16) | 1 (1) |
| Route/drug/dose | 23 (20) | 6 (5) |
| Freq/documentation | 32 (28) | 2 (2) |
| Controlled/$K^+$ | 4 (3) | 3 (3) |
| Other | 7 (6) | 0 (0) |

**Conclusion** The rate of adverse events is comparable with published work (9.5 vs 10.4) [3] but there may be significant under-reporting. However, it was considered that all major events were avoidable. The current UK Medication Safety Initiative focuses on strengthening the prescription, supply and administration of medications in the hospital setting. This study suggests that medication safety should be a priority in the ICU in 2005.

**References**

1. Audit Commission: *A Spoonful of Sugar: Medicines Management in NHS Hospitals*. Audit Commission; 2001.
2. NPSA: *7 Steps to Patient Safety – Your Guide to Safer Patient Care*. National Patient Safety Agency; 2004.
3. Leape LL, *et al.*: **Pharmacist participation on physician rounds and ADEs in the ICU.** *JAMA* 1999, **282:**267-270.

## P262

### Budget savings following a rationalisation of practice: a comparison of drug-prescribing costs in two different intensive care units

**P Campbell[1], J Murphy[1], R Forrest[2], M Garrioch[2], A Davidson[1]**
*[1]Victoria Infirmary, Glasgow, UK; [2]Southern General Hospital, Glasgow, UK*
*Critical Care* 2005, **9(Suppl 1):**P262 (DOI 10.1186/cc3325)

**Aim** To ascertain whether a comparison of drug budget spending, in comparable ICUs, could lead to a rationalisation of clinical practice and budget savings.
**Method** Two similar ICUs were chosen, both with the same bed numbers, similar patient groups, severity of admission (using APACHE II scores) and length of stay. The pharmacy departments cross-referenced the financial costs of all medications and sundries used in both ICUs. Where any major financial differences became apparent, the clinical practice related to these costs was investigated.
**Results** This budget analysis highlighted several variations in clinical practice. The main differences found were in sedation practices, the use of neuromuscular blocking drugs, antimicrobial prescribing practices and the use of differing haemofiltration sundries. The standardisation of practice in these areas led to a financial saving of over £30,000 in a year between the two units, from a combined drug budget of approximately £300,000.

**Discussion** This analysis facilitated discussion among the multidisciplinary intensive care team in an effort to improve patient care and save money at the same time. By analysing drug-prescribing costs and comparing clinical practices, we have shown that significant savings can be made. We were able to rationalise clinical practice without any significant changes in current management strategies.
Further differences in practice were also demonstrated by this study. It is hoped that, following discussions with all concerned individuals, further standardisations in practice and subsequent cost savings can be made.

## P263

## Significance and outcome of critical care system management

**S Kiatboonsri, P Charoenpan, C Kiatboonsri, P Pornsuriyasak, V Boonsrangsuk**
*Ramathibodi Hospital, Mahidol University, Bangkok, Thailand*
*Critical Care* 2005, **9(Suppl 1):**P263 (DOI 10.1186/cc3326)

**Objective** To set up a holistic critical care system.
**Background** Ramathibodi Hospital is a 1000-bed medical school, tertiary care and referral center. The ICU of the Department of Medicine was founded in 1980 and comprised six beds that served the total 132 medical inpatient beds. The ratio of ICU:total beds was thus 0.4:10. In 1990, the number of ICU beds was extended to eight, which raised the new ICU:total bed ratio to 1:10. Such a proportion of ICU beds was apparently too small. This resulted in a number of critical patients being treated in the general medical wards with difficulties in raising and maintaining the standards of critical and respiratory care. The unclear job description also deteriorated working morale and led to a rapid turnover rate among the nursing personnel.
**Steps of development** (1) In 1989–1990, attempts was made to validate the precision of the APACHE II scoring system when applied to our group of ICU patients. Among the 334 patients tested, the APACHE II scoring system was proved to be valid and the ICU performance as assessed by the Actual Death/Predicted death ratio was 1.17. (2) To estimate the actual critical care beds needed, the number of patients who were mechanically ventilated in the general wards were recorded over years (1995–1996). The data showed at least 12–20 patients were mechanically ventilated outside the ICU each day – a number that indicated the minimum additional critical care beds required. (3) In 1998, one of the 30-bed general wards was renovated to be a 20-bed intermediate care unit (IMU). The total inpatient beds was thus reduced by 10 and the new critical:total beds ratio was 2.5:10. Criteria of critical patients' admission pathways to the ICU or IMU were set. A critical care team was formed to raise and maintain standards of patient and equipment care, and to provide continued medical education in critical care medicine. A number of indices of quality control were also monitored and evaluated continuously.
**Results** Since October 1998, none of the patients who were hemodynamically unstable and/or needed ventilatory support was treated in the general ward. Despite the reduction of total inpatient beds by 10, the total number of inpatient admission has increased from 3742 in 1997 to 4657 in 2003 (24% increment). The average hospital length of stay (LOS) of the Department of Medicine has declined from 10.84 days in 1997 to 8.81 days in 2003 (18.7% reduction). The overall inpatient hospital mortality has reduced from 17.37% in 1997 to 9.90% in 2003 (43% reduction). The critical care unit performance as measured by the Actual Death/Predicted Death ratio has reduced from 1.17 in 1990 to 0.76 and 0.72 in 2002 and 2003, respectively.
**Conclusion** Our holistic critical care system management not only resulted in a better care of critical patients, but also led to an overall improvement in department performance.

## P264

## The early efficacy of CABG care delivery in a low procedure-volume community hospital: operative and midterm results

**T Papadimos**
*Medical College of Ohio, Toledo, OH, USA*
*Critical Care* 2005, **9(Suppl 1):**P264 (DOI 10.1186/cc3327)

The Leapfrog Group recommended that CABG surgery should be done at high volume hospitals (>450 per year) without corresponding surgeon-volume criteria. Recent studies have indicated that the effects of hospital volume are substantially confounded by surgeon volume, and that high surgeon volume (>125 per year) may be a more appropriate indicator of CABG quality. We thus compared operative morbidity and mortality outcomes for a low-volume hospital (LVH) (504 CABG, 2001–2003) served by five high-volume surgeons (161–285 per year) with the corresponding Society of Thoracic Surgeons (STS) national data over the same period. The LVH program implemented 'best practice' care including effective practice guidelines, protocols, data acquisition capabilities, case review process, dedicated facilities and support personnel (anesthesiology, intensivists and pharmacists). Operative mortality was similar for LVH and STS (OM: 2.38% vs 2.53%), and the corresponding LVH observed-to-expected mortality (O/E = 0.81) indicated good quality relative to the STS risk model (O/E <1). Also, these results were consistent irrespective risk category: O/E was 0, 0.9 and 1.03 for very-low risk (<1%), low risk (1–3%) and moderate-to-high risk (>3%) categories, respectively. While postoperative leg wound infections, ventilator hours, renal failure, and atrial fibrillation were increased in the LVH, the length of stay was not. The unadjusted Kaplan–Meier survival for the LVH cohort was 96%, 94%, and 92% at 1, 2, and 3 years, respectively. Our results demonstrated that high-quality CABG care can be achieved at LVH programs when served by high-volume cardiac surgeons. This approach may prove a useful paradigm to ensure high-quality CABG care and early efficacy at low-volume institutions (Table 1 shows predictors of 0-year to 3-year mortality; Cox regression).

**Table 1**

| Variable | *B* | SE | Wald | *P* value | Risk ratio | 95% CI |
|---|---|---|---|---|---|---|
| CPB time (10 min) | 0.02 | 0.00 | 16.26 | 0.0001 | 1.15 | 1.08 1.23 |
| All vein grafts | 1.75 | 0.55 | 10.15 | 0.0014 | 5.74 | 1.96 16.82 |
| Cerebrovascular disease | 1.33 | 0.43 | 9.82 | 0.0017 | 3.79 | 1.65 8.72 |
| Age (per 10 years) | 0.06 | 0.02 | 8.28 | 0.0040 | 1.63 | 1.20 1.91 |
| Redo surgery | 1.24 | 0.55 | 5.00 | 0.0254 | 3.46 | 1.17 10.26 |
| Congestive heart failure | 0.91 | 0.45 | 4.07 | 0.0435 | 2.48 | 1.03 6.00 |
| Preoperative renal failure | 1.34 | 0.76 | 3.11 | 0.0779 | 3.81 | 0.86 16.86 |

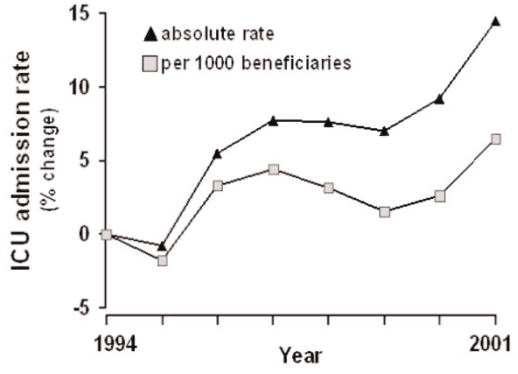
## P265

### Rising use of intensive care unit services in Medicare

**E Milbrandt[1], A Kersten[1], S Watson[1], M Rahim[1], G Clermont[1], D Angus[1], W Linde-Zwirble[2]**
*[1]The CRISMA Laboratory, Department of Critical Care Medicine, University of Pittsburgh, PA, USA; [2]ZD Associates, Perkasie, PA, USA*
*Critical Care* 2005, **9(Suppl 1):**P265 (DOI 10.1186/cc3328)

**Introduction** In recent years, rising cost, new technology, demographic shifts, and demands for higher quality have placed pressure on Medicare, the largest part of US healthcare. The consequence for the use of ICU services is unknown.
**Hypothesis** Use of ICU services is growing in the Medicare population.
**Methods** We selected all Medicare Prospective Payment System (PPS) hospitalizations from 1994 to 2001 and generated rates using corresponding beneficiary files. We calculated total ICU admission rates, rates per 1000 beneficiaries, and rates stratified by age and medical versus surgical admission.
**Results** In 1994, there were 10.7 million Medicare PPS hospitalizations, 2.2 million (20.5%) of which incurred ICU care. By 2001, hospitalizations increased 5.3% to 11.3 million, while ICU admissions increased 14.5% to 2.5 million. After adjusting for changes in the number of beneficiaries, hospitalizations fell 2.1%, while ICU admissions increased 6.4%. Those ≥ 80 years saw the greatest increase in ICU admission rates (41%), accounting for 33.4% of ICU admissions in 2001. Growth in ICU use was due to increased medical admissions, which rose 18.9% while surgical ICU admissions fell 4.7%.

**Figure 1 (abstract P265)**




**Conclusions** ICU use has been rising dramatically in Medicare, especially in the elderly. This rise is occurring despite a reduction in the number of hospitalizations per beneficiary.

## P266

### A comparative cost analysis before and after opening of an intermediate care unit

**B Solberg[1], G Ramsay[2], C Dirksen[1], F Nieman[1]**
*[1]University Hospital Maastricht, The Netherlands; [2]Atrium Medical Centre, Heerlen, The Netherlands*
*Critical Care* 2005, **9(Suppl 1):**P266 (DOI 10.1186/cc3329)

**Objective** To compare the hospital cost of intensive care patients before and after the opening of an intermediate care unit.

**Design** A before–after prospective observational study.
**Setting** University-affiliated mixed ICU, intermediate care unit (IMC) and standard wards.
**Patients and participants** A total of 1539 ICU stays were admitted from January 2001 to December 2002; 786 ICU patients were included in the study by taken a random sample. During the period before opening the IMC 329 ICU patients were included, and 457 ICU patients after opening the IMC.
**Interventions** Opening of a six-bed mixed IMC.
**Measurements and results** For each ICU patient, the following cost data were collected: total hospital cost; divided into costs during ICU stay, IMC stay and general ward stay. The total hospital cost was computed from the first ICU admission to hospital discharge. The cost of readmissions to the ICU, IMC and wards during the same hospital stay were included. Comparisons concerning costs were performed after logarithmic transformation, to improve the symmetry of distributions. The mean total hospital cost before opening the IMC was €12.961 (± 14.530) and after opening the IMC was €16.513 (± 19.324) with a significant increase of €3552 ($P$ value = 0.01) (Table 1).

**Table 1**

| Costs (€) | Before IMC ($n$) | Before IMC mean (SD) | After IMC ($n$) | After IMC mean (SD) | $P$ value (logtrans.) |
|---|---|---|---|---|---|
| ICU stay | 329 | 10,017 (13,317) | 457 | 13,020 (17,659) | 0.08 |
| IMC stay | 0 | 0 | 138 | 2612 (4060) | – |
| Ward stay | 236 | 4105 (5924) | 304 | 4065 (5095) | 0.12 |
| Total hospital stay | 329 | 12,961 (14,530) | 457 | 16,513 (19,324) | 0.01 |

Statistical relations between individual hospital cost and patient characteristics were analysed (age, gender, mortality, surgical/medical, kind of organ failure and nursing workload [TISS-28] of admission day). After correction of these variables, the increases of the hospital cost were explained by kind of organ failure ($P$ = 0.08), surgical/medical ($P$ = 0.26), and nursing workload (TISS-28) of admission day ($P$ = 0.43).
**Conclusion** This study showed an increase of total hospital cost after opening the IMC. A different patient population was admitted to the ICU after opening the IMC. More surgical patients, higher TISS score and the kind of organ failure varied between the populations before and after opening the IMC. The mean cost during the ICU stay per patient increased most (€3003).

## P267

### ICU research coordinator activities: a time-in-motion multicenter study

**E McDonald[1], F Clarke[1], C Dale[2], C Davidson[3], R Farrell[3], L Hand[1], T McArdle[3], O Smith[2], M Steinberg[2], I Watpool[3], R Ward[3], D Heels-Ansdell[1], D Cook[1]**
*[1]McMaster, Hamilton, Canada; [2]University of Toronto, Canada; [3]University of Ottawa, Canada*
*Critical Care* 2005, **9(Suppl 1):**P267 (DOI 10.1186/cc3330)

**Background** ICU Research Coordinators (ICURCs) represent a growing membership in the Canadian Critical Care Trials Group (CCCTG). The professional contribution of ICURCs to clinical critical care research is profound, but has not been well characterized.

**Objective** To describe the settings, studies, resources, tools, and activities of Canadian ICURCs.
**Methods** We conducted a prospective observational time-in-motion study of CCCTG ICURCs from 20 September to 15 October 2004. We generated items and domains in focus groups. The instrument was formatted using both open and closed ended responses. We piloted for comprehensiveness and clarity. We obtained data on the setting, studies, tools and resources available in each center, then used a weekly management log to document activities under seven domains. Completed forms were faxed to the Methods Center at St Joseph's Healthcare and entered into an Excel Spreadsheet for descriptive analyses.
**Results** Twenty ICURCs participated from 13 mixed ICUs (100% university-affiliated hospitals with 440 ± 225 hospital beds and 23 ± 11 ICU beds). Over 4 weeks in 13 ICUs, 104 ± 64 patients were admitted, 74 ± 60 were screened and 9 ± 9 were enrolled in studies. On average, there were 4.6 ± 2.1 peer reviewed, and 3.8 ± 3.5 industry studies; 5.8 ± 3.4 were RCTs, 2.8 ± 2.3 were observational and 0.8 ± 1.2 were other designs. On average, 7.1 ± 5.8 studies enrolled adults and 1.5 ± 2.4 enrolled children. These resources were accessed electronically: laboratory data (100%), diagnostic images (53.8%), radiology reports (69.2%), ECGs (15.4%) and clinical information systems (15.4%). Data collection tools include: paper (100%), NCR paper (38.5%), datafax (38.5%), laptop (7.7%), PDAs (0%), and Web-based approaches (84.6%). Time spent in each of seven activities was: study preparation (literature review, inhouse protocol development, REB submissions and amendments, budget preparation, CRF development and piloting, regulatory document assembly, in-services), 16.5%; research conduct (screening, consent and family meetings, pharmacy and other study supplies, data collection and queries, conducting and preparing tests, AE and SAE reporting, bedside protocol compliance), 44.1%; communication (email/telephone calls/mail, staff education), 14.3%; management (team meetings, multicentered management, screening and finance logs, initiation audit and close-out visits), 13.5%; data management (database creation and data entry, analysis), 3.9%; dissemination (interim and final reports, conference preparation and presentation), 3.0%; and miscellaneous, 4.7%.
**Conclusions** CCCTG ICURCs work primarily in mixed university-affiliated ICUs, conducting randomized trials in adults. The availability of electronic resources is modest, and variable data collection methods are employed. ICURCs engage in many activities to prepare, implement, and manage investigations for critically ill patients.
**Acknowledgements** This study was funded by Father Sean O'Sullivan Research Center and the Canadian Institutes for Health Research.

## P268

### Impact of critical care outreach on cardiac arrest rates and readmission rates in an adult cardiothoracic centre

**P Wilton, C Carbery, J Farrimond, J Mitchell, J Hall, T Apps**
*Royal Brompton & Harefield NHS Trust, Harefield, UK*
*Critical Care* 2005, **9(Suppl 1):**P268 (DOI 10.1186/cc3331)

**Introduction** Following the recommendations of *Comprehensive Critical Care* [1], outreach services have been implemented nationally with the remit of avoiding admission to intensive care; facilitating discharge of critically ill patients from Level 3 areas and educating ward staff in critical care skills. This initiative consumes significant resources, and to date there has been disappointing evidence that this investment has been worthwhile in terms of improving outcomes, reduction in cardiac arrests, and unplanned admissions to intensive care.
**Objective** This audit aims to identify whether the implementation of an outreach team has had an impact on inhospital cardiac arrest rates and readmission rates to ICU.
**Methods** A retrospective analysis of the ICU and outreach database was performed to quantify the readmission rate within 48 hours due to organ failure and the inhospital cardiac arrest rate. This analysis was performed 1 year pre and post the implementation of a dedicated nurse-led outreach team.
**Results** Cardiac arrest rate has reduced by 40% since the introduction of the outreach service. The readmission rate within 48 hours with organ failure was less than 2%.
**Conclusion** We report a reduction in the cardiac arrest rate post implementation of outreach, although this may be due to other external factors. The readmission rate within 48 hours of ICU discharge is low, reflecting an appropriate and effectively facilitated discharge practice.
**Reference**
1. DoH: *Comprehensive Critical Care: A Review of Adult Critical Care Services*. Department of Health; 2000.

## P269

### Critical care outreach: implementation in a cardiothoracic centre

**C Carbery, P Wilton, J Farrimond, J Mitchell, J Hall, T Apps**
*Royal Brompton & Harefield NHS, Harefield, UK*
*Critical Care* 2005, **9(Suppl 1):**P269 (DOI 10.1186/cc3332)

**Introduction** Outreach teams have recently been implemented across the United Kingdom with a remit to deliver a specialist level of assessment and intervention with the ward setting. These goals include early identification of deteriorating patients to avert admission to ICU; facilitating discharge from ICU and education of ward staff.
**Objective** An evaluation of a nurse-led outreach team to facilitate the threefold remit of outreach in a specialist cardiothoracic unit.
**Methods** Establishment of a unique referral criteria to reflect the specialist cardiothoracic casemix. One hundred per cent of Level 3 discharges are followed up and actively managed to facilitate early discharge (including patient on intermittent haemofiltration, intermittent CPAP, tracheostomies *in situ* and low levels of inotropic support). Ward-based education programme. Electronic data collection.
**Results** Over 800 patients were reviewed over a 12-month period encompassing more than 2000 patient assessments. Level 3 discharge follow-up increased to 100% from 45% prior to establishment of a dedicated team. The overall readmission rate has remained unchanged; however, the readmission rate within 48 hours with organ failure is below 2%, reflecting appropriate discharge from Level 3. Forty-five per cent of patients showed biochemical evidence of renal impairment post ICU discharge requiring a longer stay on outreach.
**Conclusion** This evaluation has highlighted the increasing dependency of patients managed outside of ICU. Facilitating ICU discharge and follow-up of patients with renal and respiratory impairment impacts significantly on ICU length of stay.

## P270

### A 'Count Outreach Warning Score' forecasts need for 'step-up' care

**M Kuper, J Adams, S Singh, A Blay, N Soni**
*Chelsea Hospital, London, UK*
*Critical Care* 2005, **9(Suppl 1):**P270 (DOI 10.1186/cc3333)

**Objective** The number of physiological abnormalities predicts mortality [1], so we defined a positive 'Count Outreach Warning Score' (COWS) as three or more physiological abnormalities

**Table 1 (abstract P270)**

| Test | PART | PART | EWS | EWS | MEWS | MEWS | COWS | COWS |
|---|---|---|---|---|---|---|---|---|
| Test says … | 'Sick' | 'Well' | 'Sick' | 'Well' | 'Sick' | 'Well' | 'Sick' | 'Well' |
| 'Stepped-up' | 2 | 15 | 6 | 11 | 6 | 11 | 10 | 7 |
| Normal care | 0 | 62 | 2 | 60 | 2 | 60 | 2 | 60 |
| Sensitivity | 2/17 = 12% | 95% CR 21–40 | 6/17 = 35% | 95% CR 20–44 | 6/17 = 35% | 95% CR 20–44 | 10/17 = 59% | 95% CR 41–70 |
| Specificity | 62/62 = 100% | 95% CR 98–100 | 60/62 = 97% | 95% CR 92–99 | 60/62 = 97% | 95% CR 92–99 | 60/62 = 97% | 95% CR 92–99 |

(temperature < 35°C or > 39°C; saturation < 95%; urine output below 30 ml/hour; heart rate > 99 or < 51, respiratory rate >19, mental state V/P/U [i.e. not alert]). Could COWS forecast the need for 'step-up' from normal ward care?

**Method** All observations on the 79 patients present on one medical and one surgical ward over 7 days at the Chelsea and Westminster Hospital, London were scored using COWS and also the published scores EWS, MEWS and PART. A patient was predicted 'sick' by a score given a positive result on any one set of observations. Outcome was followed for 28 days. 'Stepped-up' care was prospectively defined as any of intensive care, high dependency or outreach referral or admission, cardiac arrest, death, or placement of a 'do not resuscitate' order. Confidence intervals were calculated by constant chi-squared boundaries and sensitivities compared with McNemar's test.

**Results** Of 79 patients studied, 17 required 'step-up' from normal ward care (Table 1). COWS appeared more sensitive at predicting 'step-up' ($P = 0.06$), with similar specificity to the other scores. In four patients correctly identified by more than one score, COWS became positive 4–24 hours earlier whereas only one patient was identified by another score before identification by COWS.

**Conclusion** COWS forecast the requirement for 'step-up' care earlier and with more sensitivity than previous scores.

**Reference**

1. Goldhill D, McNarry A: *BJA* 2004. **92:**882.

## P271

### First national survey on the use of the Internet and other electronic resources among Spanish intensivists

**V Gómez Tello[1], N de Lucas[2], J Añón[3], E Palencia[4], J Latour[5], R Díaz Alersi[6]**

*[1]Clínica Moncloa, Madrid, Spain; [2]Hospital San Rafael, Madrid, Spain; [3]Hospital Virgen de la Luz, Cuenca, Spain; [4]Hospital Gregorio Marañón, Madrid, Spain; [5]Hospital General Universitario, Elche, Spain; [6]Hospital de Puerto Real, Cádiz, Spain*

*Critical Care* 2005, **9(Suppl 1):**P271 (DOI 10.1186/cc3334)

**Objective** To assess Spanish intensivists' knowledge and use of different electronic resources; the Internet, electronic mail, mailing lists and portable electronic devices (PDAs).

**Design** A cross-sectional survey.

**Participants** Eight hundred and twenty Spanish intensivists were contacted by hospital commercial delegates of a pharmaceutical company. The survey was simultaneously published in electronic forums.

**Methods and results** A total of 682 responses were obtained (response rate: 73.9%). The Internet was used autonomously by 95.7% ($n = 653$) of responding physicians and 78.8% ($n = 513$) were autodidactic in this field. Learning gaps were reported by 66.7% ($n = 451$) of the respondents and up to 58.3% ($n = 398$) acknowledged at least two deficit areas. The responses from female intensivists showed lower Internet use and greater learning gaps in at least one area (odds ratio [OR] 2.44; confidence interval [CI] 1.5–3.95).

The Internet was the second most frequent source for clinical consultation (60.9%; $n = 409$), only preceded by peer consultation with ICU colleagues (65.2%; $n = 438$). The most frequently visited webpages were bibliographical databases (64.5%; $n = 412$) and electronic journals (63.4%; $n = 405$). EBM pages were rarely visited (18.9%; $n = 421$). In fact, the number of different types of websites was the main factor associated with solving clinical questions by the Internet (OR 1.37; CI 1.25–1.5).

Email correspondence was used by 92.4% ($n = 630$) of those surveyed and 89.6% ($n = 611$) used it for professional purposes, but 25.3% ($n = 159$) admitted to ignoring its full potential. Email correspondence as a resource correlated inversely with age (OR 0.95; CI 0.92–0.99; $P = 0.015$).

Electronic mailing lists were used by 62.3% ($n = 425$) of the intensivists. Of the remainder, 41.7% ($n = 113$) were not familiar with them and 31.7% ($n = 86$) reported insufficient expertise to manage them correctly. Only 20.1% ($n = 136$) own portable electronic devices. However, 63.5% ($n = 416$) considered these devices would be a useful tool for immediate consultations at the bedside. Female respondents were less predisposed towards their use (OR 2.44; CI 1.5–3.95; $P = 0.0002$).

An index of five punctuated items was elaborated to summarize in a single variable the use of all resources: preferable access to the Internet to solve clinical questions (one point); Internet consultation two or more times per week (one point); electronic mailing list consultation two or more times per week (one point); intensive care mailing list consultation (one point); and use of at least one medical software program in the PDA (one point). The variables associated with a low score in this index were: female gender, increase of age, educational character of the hospital and being a resident physician.

**Conclusions** A majority of Spanish intensivists uses the Internet and electronic mail. Important educational deficits exist and a clear underuse of fundamental webpage sources has been observed. Mailing lists and portable devices are not prevalent electronic resources. Training courses and educational programs are needed to encourage and facilitate the use of these resources and to promote email lists. Special attention needs to be directed at female intensivists who seem to be more reluctant to access these resources.

## P272

### Critical illness polyneuromyopathy: a major problem in a general intensive care unit

**S Nanas, K Kritikos, E Angelopoulos, C Routsi, S Tsikriki, S Dimopoulos, M Pratikaki, T Loukas, E Papadopoulos, I Floros, C Roussos**

*Critical Care Department, Medical School, National and Kapodistrian University, Evangelismos Hospital, Athens, Greece*

*Critical Care* 2005, **9(Suppl 1):**P272 (DOI 10.1186/cc3335)

**Introduction** Critical illness polyneuromyopathy (CIPM) constitutes a significant cause of difficulty in weaning patients from the ventilator, prolongation of their stay in the ICU and increased

morbidity and mortality. No reliable global epidemiologic data exist to define the overall prevalence and incidence of CIPM in ICU patients.

**Objectives** To estimate the clinical incidence and prevalence of CIPM in the general ICU setting.

**Patients and methods** From August to December 2004, 205 consecutive admissions in a 25-bed university general ICU were evaluated. Thirty-four patients were discharged in less than 24 hours from admission and were excluded from the study. The remaining 171 patients (119 males, 52 females, mean age: 52 ± 18 years) were assigned admission APACHE II (17 ± 8) and SOFA (7 ± 3) scores and were evaluated for the development of new onset polyneuromyopathy, detected by assessing muscle strength reduction (by the Medical Research Council scale), reduced/absent deep tendon reflexes, sensory involvement and clinically evident muscle wasting. Biochemical parameters and drug treatment were evaluated daily. Other possible causes of acute weakness appearing after ICU admission were excluded. Prevalence of CIPM was estimated clinically on two different occasions. All continuous variables are presented as the mean ± standard deviation.

**Results** Twenty (12%) out of the 171 enrolled patients developed CIPM. One hundred and five patients (71 males, 34 females) had an ICU stay of more than 7 days, with an admission APACHE II score of 18 ± 7 and a SOFA score of 8 ± 3. Nineteen percent of those patients developed CIPM. All affected patients had an ICU stay of more than 7 days. Patients with CIPM (13 males, seven females) had a higher admission APACHE II (21 ± 8 vs 16 ± 7; $P < 0.02$) and SOFA (82 vs 7 ± 3; $P = 0.05$) score and a longer ICU stay (29 ± 21 vs 12 ± 13 days; $P < 0.001$) than those without CIPM (151 patients). The overall mortality rate was 22%. Thirty-five percent of patients with CIPM died during their ICU stay, compared with 21% of patients without CIPM. Regarding age, no statistically significant difference was found among the two groups. Prevalence of CIPM in the ICU was estimated to be 20%.

**Conclusions** Previous prospective studies have reported higher incidence rates for CIPM by studying subgroups of patients with severe sepsis/systemic inflammatory response syndrome. Our data show a high incidence and prevalence of CIPM in a general consecutive ICU population. This finding clearly illustrates the need for a longer prospective study to investigate the pathophysiologic mechanisms, as well as the risk factors involved.

## P273

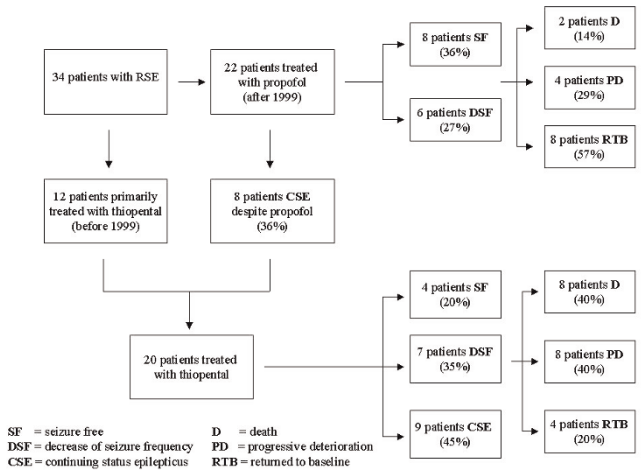
### Propofol and thiopental for refractory status epilepticus in children

**S van Gestel, H Blusse van Oud-Alblas, M Malingre, T Ververs, K Braun, O van Nieuwenhuizen**
*UMC Utrecht, Wilhelmina Children's Hospital, Utrecht, The Netherlands*
*Critical Care* 2005, **9(Suppl 1):**P273 (DOI 10.1186/cc3336)

**Introduction** Thiopental is commonly used as a last treatment modality in case of refractory status epilepticus (RSE). Its side effects are well known, but there is little information about the frequency in which they occur and the impact they have on clinical practice. Because of the adverse effects of thiopental, several guidelines recommend propofol as an alternative therapy before thiopental is started. However, propofol is associated with potentially fatal outcome, and its efficacy in the treatment of RSE is almost exclusively based on small case series and case reports.

**Objective** The purpose of this study was to assess safety and efficacy of propofol and thiopental in the treatment of RSE in children.

**Figure 1 (abstract 273)**




**Setting** A pediatric intensive care unit of a tertiary teaching hospital.

**Methods** Retrospective data collection of all patients treated with propofol or thiopental for RSE between January 1993 and January 2004. Before 1999, patients were treated with thiopental, when phenytoin and high doses of midazolam had failed to terminate the status. After 1999, propofol was administered systematically to all children before thiopental was started, reserving thiopental for those who suffered from side effects of propofol or did not respond to it. The maximum dose of propofol never exceeded 5 mg/kg/hour. Success and adverse effects of treatment were noted and short-term seizure control and neurological outcome were assessed.

**Results** Thirty-three patients were treated for 34 episodes of RSE. The effects of propofol and thiopental on seizure activity and short-term neurological outcome are shown in Fig. 1. Propofol was used on 22 occasions. Side effects were infrequent, of limited severity and fully reversible. Mortality was low and attributed to the severity of the underlying disorder. Twenty children were treated with thiopental. Hemodynamic instability occurred in most patients, but could be adequately managed with extra fluids and vasoactive medication. The majority of patients developed fever, pleural effusions and infiltrates on their chest X-ray, suggestive of pneumonia. Bacterial cultures, however, often remained negative.

**Conclusions** Propofol is a safe and effective treatment option for RSE in children. When treatment with propofol fails and thiopental is indicated, a broad range of complications can be encountered. We advise using propofol before thiopental is started.

## P274

### Therapeutic window of opportunity assessment in antithrombotic therapy, using a glycoprotein IIb/IIIa inhibitor (tirofiban), in an experimental model of acute ischemic embolic stroke in rabbits

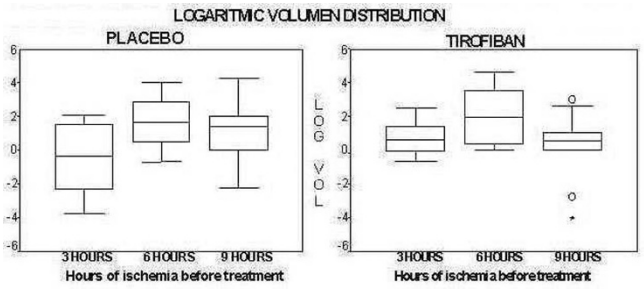
**V Segura Lemus, R Alfaro Ponce, J Castellanos Gonzalez, R Tenze Epperson, F Sansivirini Valle, N Astacio Soria**
*Universidad Dr Jose Matias Delgado, Antiguo Cuscatlan, El Salvador*
*Critical Care* 2005, **9(Suppl 1):**P274 (DOI 10.1186/cc3337)

**Background** Preliminary preclinical and clinical studies have established efficacy in the use of GP IIb/IIIa inhibitors in the treatment of acute ischemic stroke. This study was designed to

**Figure 1 (abstract P274)**

| Groups | Sub-Groups | N | Volume median | Neuroscore 24h | Neuroscore 48h | ICH |
|---|---|---|---|---|---|---|
| 3 Hours | PLACEBO | 12 | 0.6892 | 8 | 8 | 0% |
| | TIROFIBAN | 8 | 1.8481 | 8 | 8 | 0% |
| 6 Hours | PLACEBO | 12 | 5.4880 | 9 | 9 | 0% |
| | TIROFIBAN | 10 | 7.5492 | 9 | 9 | 0% |
| 9 Hours | PLACEBO | 15 | 4.0841 | 8 | 9 | 6.67% (1) |
| | TIROFIBAN | 14 | 1.7549 | 8.5 | 9 | 0% |

**Figure 2 (abstract P274)**




assess the therapeutic window of opportunity of tirofiban in stroke and the risk of intracerebral hemorrhage (ICH).

**Methods** We conducted a randomized, double-blind, placebo-controlled, experimental preclinical trial. Seventy-one male New Zealand white rabbits were included in the study. Rabbits were embolized by injecting an autologous fibrin-rich blood clot incubated for 22 hours into the common right carotid artery. Rabbits were divided into three groups (3, 6, and 9 hours of ischemia). Each one was randomly divided into two subgroups, placebo and tirofiban (0.4 μg/kg/hour) parenterally infused for 30 min. A neuroscore was performed 24 and 48 hours postembolization. Postmortem pathologic analysis measured infarct volume and ICH.

**Results** Analysis of variance analysis showed a significant difference between the volumes of the 3 and 9 hours groups compared with the 6 hours group ($P = 0.005$, power = 85.9%); there was no significant difference between the placebo and tirofiban subgroups ($P = 0.552$, power = 9.1%). No significant difference was found among the three groups between placebo and tirofiban ($P = 0.109$, power = 45.1). Incidence of ICH was 1.4%. Median analysis showed a rise of the infarcted volume in the subgroups between 3 and 6 hours and a decline between 6 and 9 hours was more evident in the tirofiban subgroup. There was no significant difference in neuroscores among subgroups.

**Conclusions** There is no statistical significant difference between tirofiban and placebo in reducing the infarct volume, but the results obtained give the impression that tirofiban used in longer periods of ischemia (> 6 hours) starts to show an effect in reducing the size of the infarct. This result points out that tirofiban administered after 6 hours might reduce the infarct by blocking microthrombosis, and protecting the penumbra area to convert in necrosis. No significative difference was found in the clinical outcome. Tirofiban does not increase the incidence of ICH. Further studies need to be made to establish significant differences in order to obtain conclusive results.

## P275

### Hemodynamic instability following bilateral carotid endarterectomy

**R Govindarajan, N Kodali, J Aronsohn, N Elshamma, A Samaan, J Thomas, M Fam**
*Brookdale University Hospital & Medical Center, Brooklyn, NY, USA*
*Critical Care* 2005, **9(Suppl 1):**P275 (DOI 10.1186/cc3338)

**Background** Blood pressure (BP) and heart rate (HR) instability following carotid endarterectomy (CEA) have been extensively documented in the literature [1,2]. CEA has been associated with disturbance of the baroreceptor control mechanism caused by surgery in the carotid sinus region [1]. Smit and colleagues reported bilateral carotid sinus denervation producing long-term blood pressure variability [3]. In our study, we report finding profound hemodynamic instability during the 24-hour period following CEA on four patients who had undergone a previous contralateral CEA (Group 1) and compare management of these patients with five controls who underwent CEA without previous contralateral CEA surgery (Group 2).

**Methods** All patients underwent general endotracheal anesthesia with the same induction and maintenance regimen. BP and HR were recorded continuously perioperatively and for 24 hours postoperatively. Incidence of postoperative hypertension (HTN), hypotension, bradycardia, maximal increase in HR and the associated use of corrective medications were recorded.

**Results** The incidence of refractory hypotension and bradycardia was higher in the bilateral CEA group (Group 1, $n = 3/4$), while in the unilateral CEA group (Group 2) hypotensive and bradycardic response was transient and readily reversible. All patients exhibiting refractory hemodynamic instability in Group 1 required aggressive management with sympathomimetic and parasympatholytic medications for a period of 24–36 hours postprocedure in the PACU and SICU. Hypertension was a prominent feature in three patients in Group 2 ($n = 3/5$) while one patient in Group 2 developed cardiac dysrhythmia that required cardioversion. Only one patient in both groups needed hospitalization longer than 72 hours on account of recurrent cardiac dysrhythmia.

**Conclusion** Not withstanding the small sample size, our results indicate that bilateral CEA is associated with significant hemodynamic instability and often requires aggressive pharmacotherapy. Awareness, early diagnosis and prompt treatment improve outcome and often single out patients who need closer follow-up during the posthospitalization period. Our data showed that hemodynamic instability does not significantly affect early discharge [4] while intraoperative injection of bupivicaine at the carotid sinus level does not reduce the level of postoperative hypotension.

**References**

1. *J Vasc Surg* 2002, **36:**793-798.
2. *Stroke* 1996, **27:**1167-1172.
3. *Circulation* 2002, **19:**1329-1335.
4. *Cardiovasc Surg* 1998, **6:**470-474.

## P276

### New presentations about risk factors of ischemic stroke in young persons

**I Ustyantseva, T Vizilo, O Khokhlova, E Belogortseva, I Pisareva, G Agadzhanyan**
*Federal State Medical Prophylactic Institution Scientific Clinical Center, Leninsk-Kuznetsky, Russia*
*Critical Care* 2005, **9(Suppl 1):**P276 (DOI 10.1186/cc3339)

The aim of the study was the demonstration of risk factors in young persons who have an acute disorder of the cerebral circulation.

We examined 13 patients aged 42–49 years old and two children (9 and 11 years old) with verified diagnosis of acute disorder of the cerebral circulation by ischemic type during an acute period of the disease. The control group consisted of 10 healthy persons aged 40–50 years old.
Homocysteine, erythropoietin and cytokine concentrations in the blood serum were detected by the immunochemiluminescent analyzer 'IMMULITE' (USA). The values of the lipid metabolism (common cholesterol, different density lipoproteins, triglycerides, B lipoproteins) were detected by the analyzer 'HITACHI-912' (Japan). To determine the rheologic properties of the blood we investigated its viscosity by the rotation viscometer ABR-2 (Russia). Fibrinogen concentration was detected by the coagulograph ACL-100 (Italy). The significant differences between groups were detected by Student and Wilkoxon–Mann–Whitney criteria.
The study resulted in the observation of moderate hyperhomocysteinemia, atherogenic dislipidemia, blood rheologic properties and erythropoesis, pathology, and immune system disorders. Patients with hyperhomocysteinemia did not have common risk factors; their ischemic stroke had pathogenetic features: atherothrombotic subtype, with interrupted step onset and gradual growing of the symptoms during several hours or days with expressed neurological deficit. Examined children had a homocysteine concentration in blood serum of 18.4 ± 10.4 μmol/l, versus 4.66 ± 0.31 μmol/l in healthy children at the compared age. The main risk factor in young persons with ischemic stroke's atherothrombotic subtype is thus an increased level of homocysteine.

## P277

## Social problems in the management of acute ischemic stroke

**K Ishii[1], H Kobayashi[1], H Nagatomi[2]**
*[1]Oita University Faculty of Medicine, Oita, Japan; [2]Nagatomi Neurosurgical Hospital, Oita, Japan*
*Critical Care* 2005, **9(Suppl 1):**P277 (DOI 10.1186/cc3340)

**Purpose** The efficacy of thrombolysis, systemic t-PA or local transarterial urokinase infusion in the ischemic stroke of acute stage has recently been proved. However, the patients brought to the stroke center during the 'Golden time' are still not numerous. To elucidate this problem, we analyzed the process until hospitalization after the onset of symptoms.
**Methods** The clinical subjects consisted of 335 consecutive patients with ischemic stroke in the acute stage, hospitalized in our hospital, between April 2003 and March 2004. We investigated clinical course, especially, the time from the onset to the physical examination, and radiological examinations (CT, MRI, MRA and/or cerebral angiography). The mean age was 72.1 years. Among them, 99 patients were classified as atherothrombosis, 72 were cardiac embolism, 134 were lacunar infarction and 30 were transient ischemic attack. Only seven patients underwent local urokinase thrombolysis.
**Results** Eighty-six patients (25.7%) were hospitalized within 3 hours from the onset, and 135 patients (40.3%) were within 6 hours. Among these 135 patients, only 58 were admitted by ambulance. We found the following results. The main reason for the delayed admission is through another hospital, not the stroke center. The patients denying their symptoms is not so rare. The patients or their family often hesitate to request the emergency car.
**Conclusions** We should educate citizens more for the warning signs of ischemic stroke and also the necessity of emergency admission and therapy. In addition, we should justly build a core stroke center in the district and centralize the patients.

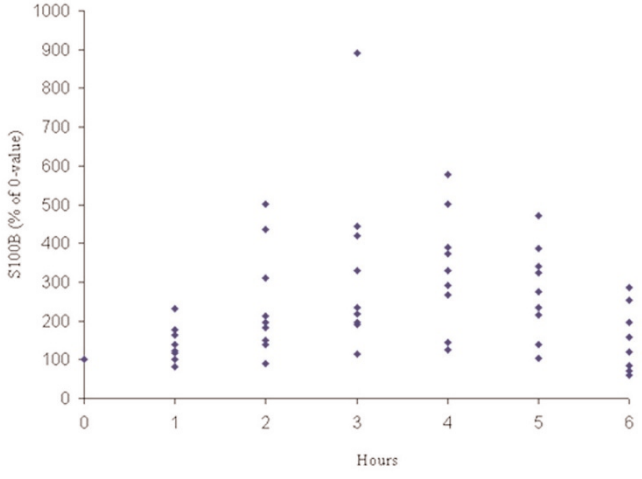
## P278

## Blood–brain barrier damage is an early event in porcine endotoxemic shock

**M Lipcsey[1], A Larsson[2], J Sjölin[3], L Hansson[2], M Eriksson[1]**
*[1]Akademiska Sjukhuset, Uppsala, Sweden; [2]Section of Clinical Chemistry, Department of Medical Sciences, Uppsala, Sweden; [3]Section of Infectious Diseases, Department of Medical Sciences, Uppsala, Sweden*
*Critical Care* 2005, **9(Suppl 1):**P278 (DOI 10.1186/cc3341)

**Background** Cerebral dysfunction is frequently seen in septic shock and correlates to outcome. The pathogenesis of the cerebral dysfunction is unknown. We decided to study the effects of experimental septic shock on cerebral damage, as evaluated by the serum levels of S100B, a well-established marker for brain and blood–brain barrier damage.
**Materials and methods** Endotoxemic shock was induced in 10 anesthetized domestic piglets by an infusion of *Escherichia coli* endotoxin. Blood samples for hemoglobin and S100 B measurements were taken at baseline and repeated hourly. After 6 hours, the piglets were sacrificed. S-100B was measured by sandwich ELISA.
**Results** All animals had very low S100B values at baseline. There were significant increases in S-100B at 1–5 hours in comparison with the baseline values. The increases in S100B were most expressed at 3 hours, at which time point the levels were increased up to ninefold ($P < 0.05$). Changes in hemoglobin levels reflected an increased vascular permeability during endotoxemic challenge. The magnitude of the increase in hemoglobin, was considerably less expressed than those of S100B.
**Conclusion** Anesthesia does not *per se* induce these changes in our pig model. The increase of S100B found in this study thus shows that there is minor blood–brain barrier damage occurring already during the first hours of porcine endotoxemic shock. Serum samples of S100B may be an alternative to cerebrospinal fluids in evaluating blood–brain barrier damage. Such sampling may, in certain selected cases, even turn out to be of value in clinical practice, as spinal puncture is hazardous to perform in patients with coagulation disturbances (e.g. in septic shock).

**Figure 1 (abstract P278)**



## P279

### Antiapoptotic effects of delta opioid peptide [D-Ala2,D-Leu5]enkephalin in brain slices induced by oxygen-glucose deprivation

**XR Wang[1], YJ Zheng[1], HZ Chen[2], XJ Wu[2], YH Zhao[1], DS Su[1]**
*[1]Department of Anesthesiology, Renji Hospital, Shanghai Second Medical University, Shanghai, China; [2]Department of Pharmacology, Shanghai Second Medical University, Shanghai, China*
*Critical Care* 2005, **9(Suppl 1):**P279 (DOI 10.1186/cc3342)

**Background** Delta opioid peptide [D-Ala2,D-Leu5]enkephalin (DADLE) has been shown to play a role in neuronal protection against hypoxic ischemia. However, the cellular mechanisms of these actions of DADLE on neurons are not totally clear. Being an *in vitro* model of brain ischemia, oxygen-glucose deprivation (OGD) injury in rat brain slices has the advantages of both *in vivo* and *in vitro* models, and therefore can imitate damages induced by brain I/R injury in intact animals. In the present study, we examined the protective mechanism(s) of DADLE against apoptosis using a rat brain slice model. In addition, we determined whether delta-opioid receptors are unique and have a specific role in neuroprotection against OGD injury by activating the MAPK pathway, specifically through delta2-opioid receptors.
**Methods** The brain slices were incubated with different concentrations of DADLE after injury by OGD. Selective delta2-opioid antagonist or selective inhibitor of ERK kinase was co-incubated with or without DADLE. The effects of DADLE against apoptosis in neurons were measured by the following biochemical and morphological assays: LDH release, RT-PCR, western blot, and TUNEL staining.
**Results** OGD caused LDH release in brain slices. DADLE inhibited OGD-induced LDH release. Naloxone, and naltriben methane sulfonate, partially suppressed the survival of brain slices promoted by 10 μM DADLE. DADLE at lower concentrations ($10^{-6}$ and $10^{-5}$ M) significantly suppressed Bax mRNA expression and enhanced Bcl-2 mRNA expression. But with the increased concentrations of DADLE, the ability to regulate apoptotic gene expression was attenuated. DADLE induced ERK phosphorylation in brain slices with the increase of concentrations. The withdrawal of oxygen and glucose *per se* decreased the ERK phosphorylation. In the absence of oxygen and glucose, DADLE at $10^{-5}$ M concentrations could, however, increase the ERK phosphorylation. Naltrindole reduced the degree of ERK phosphorylation induced by $10^{-5}$ M DADLE. PD98059 abolished the DADLE-induced phosphorylation of ERK in the condition of OGD. PD98059 not only abolished the cell survival promoted by DADLE, but also apparently led to a higher level of LDH release when compared with the DADLE control.
**Conclusions** Our results suggest, therefore, that endogenous opioid peptides may, at low concentrations, promote cell survival via the MEK–ERK pathway, perhaps through delta2-opioid receptors.

## P280

### The use of transcranial Doppler ultrasonography in early outcome prediction of patients with subarachnoid hemorrhage

**A Lavrentieva, B Soulountzi, B Boutsas, A Lampanari, A Mitka, M Bitzani**
*G Papanikolau Hospital – ICU, Theesaloniki, Greece*
*Critical Care* 2005, **9(Suppl 1):**P280 (DOI 10.1186/cc3343)

**Introduction** Transcranial Doppler ultrasonography (TCD) is a well-established technique for detection of cerebral vasospasm in patients with subarachnoid hemorrhage (SAH). The aim of our study is to investigate whether there is a relationship between TCD findings during the first 3 days after admission and the neurological outcome of patients.
**Materials and methods** Sixty-seven patients (60 ± 12.9 years, APACHE II score 18.2 ± 6.4) were included in our study. TCD middle cerebral artery systolic (SV), diastolic, and mean flow velocities and pulsatility index (PI) were measured daily following SAH. Neurological evaluation was performed at ICU discharge using the Glasgow Outcome Score (GOS). A GOS score of 1–3 was considered a pure outcome (group 1, $n = 56$), a GOS score of 4 or 5 as a good outcome (group 2, $n = 11$).The Student $t$ test was used to compare the data and $P < 0.05$ was considered significant.
**Results** See Table 1. At admission there was no statistically significant difference between the two groups in their flow velocities and PI. The patients with pure outcome (group 1) exhibited higher systolic flow velocities and higher PI on day 3 after admission.

**Table 1**

**TCD findings during the first 3 days after SAH (mean ± standard deviation)**

| | Day 1 | | Day 2 | | Day 3 | |
|---|---|---|---|---|---|---|
| | PI | SV | PI | SV | PI | SV |
| Group 1 | 1.4 ± 0.6 | 74 ± 30 | 1.26 ± 0.4 | 88 ± 35 | 1.63 ± 0.6 | 106 ± 4 |
| Group 2 | 1.17 ± 0.3 | 60 ± 18 | 1.21 ± 0.16 | 68 ± 8 | 1 ± 0.07 | 57 ± 9 |
| *P* | NS | NS | NS | NS | < 0.05 | < 0.05 |

NS, not significant.

**Conclusion** The elevation of PI and systolic flow velocity on day 3 after admission seems to be related to pure neurological outcome of patients suffering SAH probably due to early appearance of vasospasm.

## P281

### OCTOPUS – observation or computed tomography of mild head injury in Sweden: a randomised clinical trial concerning effects and costs

**J af Geijerstam[1], S Oredsson[2], M Britton[1]**
*[1]Department of Medicine, Karolinska University Hospital, Stockholm, Sweden; [2]Helsingborg Hospital, Helsingborg, Sweden*
*Critical Care* 2005, **9(Suppl 1):**P281 (DOI 10.1186/cc3344)

**Background** Mild head injury, defined as short-term loss of consciousness and/or amnesia as a result of head trauma, is a common problem in emergency departments worldwide. Acute computed tomography (CT) in triage for admission as well as inhospital observation is suggested as standard practice for these patients. However, the outcome, safety and costs of the two strategies is unclear. To address this question a randomised controlled trial (RCT) was conducted.
**Methods** A multicenter, pragmatic RCT with 39 emergency departments throughout Sweden participating to randomise the 2500 cases needed. *Eligibility criteria* Head trauma within the past 24 hours, age 6 years or older, confirmed or suspected amnesia or brief loss of consciousness, GCS 15, normal neurological findings and no associated injuries that require admission. *Randomisation* Urgent CT for all patients, early discharge for home care if normal findings. Admission for inhospital observation. *Main hypotheses* Medical outcome – the CT strategy is safe and clinically equivalent to one based on inhospital observation. Cost comparison – the CT

strategy reduces costs for management of mild head injury in the acute stage. Costs in the follow-up period are equivalent between the strategies. *Endpoints* Medical outcome – patient function at 3 months (Glasgow Outcome Scale Extended). Cost comparison – resource utilisation in acute and follow-up phase.
**Results** From May 2001 through January 2004, 2603 patients underwent randomisation. Patient follow-up was completed in June 2004. Data on the primary endpoint (GOSE at 3 months) are available for 97% of the cases. Data analysis and manuscript preparation are currently under way.
**Conclusions** The OCTOPUS study has randomised over 2600 patients with mild head injury to acute CT to triage for admission or inhospital observation. Results from the study regarding the medical effects, safety and costs of the two strategies will be available in late 2005. Data on group characteristics and practical performance will be presented at ISICEM in March 2005.

## P282

### Post-trauma subarachnoid hemorrhage

**C Kaddour, R Souissi, M Laamourou, Z Haddad**
*National Institute of Neurology, Tunis, Tunisia*
*Critical Care* 2005, **9(Suppl 1):**P282 (DOI 10.1186/cc3345)

**Purpose** Assessment of the incidence of coronary complication during post-trauma subarachnoïd hemorrhage (SAH).
**Methods** An open, double-blind, prospective study, during a period of 15 months in the Department of Anesthesia and Resuscitation of the National Institute of Neurology of Tunis.
**Patients** Thirty-five patients with head trauma in whom a CT scan reveals a SAH on admission. Patients with cardiovascular history, thorax trauma, neurological coma related to a vascular pathology and non-neurological coma were excluded.
**Results** The mean age of patients is 39 ± 17 years; 85% had a Glasgow Coma Scale < 8 on admission. The mean ISS was 27 ± 14, and 6% and 54% had a Fischer scale between 3 and 4, on admission. Electrocardiogram changes in 57% of patients. Troubles of repolarization are the most frequent; 94% of patients presented this trouble on the third day. The mean duration of these troubles is 4 ± 1 days. Over the three performed measurements, total CPK was increased in 88% of patients, creatine kinase MB isoenzyme was increased in 65% of patients and Troponin Ic was elevated in 34% of patients in a certain time of the evolution with an average of 0.068 (± 0.2). The peak of Troponin Ic occurred on the third day with an average of 0.113 (± 0.338). The increase of Troponin Ic is associated with a poor CT scan grade. The elevation of Troponin Ic is correlated with T-wave anomalies in comparison with those of the ST segment. But it is not correlated to creatine kinase MB elevation. The T-wave troubles, which are more frequent, therefore reflect better a myocardic lesion and Troponin Ic compared with creatine kinase MB is a better indicator of myocardic ischemia during SAH. In our department, no case of mortality was related to a cardiac cause. The incidence of Troponin Ic and T-wave troubles could be considered predictive factors of mortality.
**Conclusion** According to this study, troubles of repolarization during post-trauma SAH are frequent in the acute phase of the first 3 days. They could reflect a myocardic lesion as it is indicated by the increase of Troponin Ic, which is associated with severe neurological injuries.

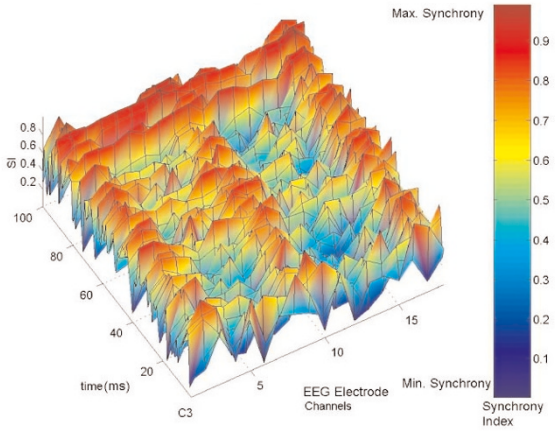
## P283

### Multimodal neuroelectrophysiological studies to predict outcome in paediatric patients with traumatic brain injury

**M Gray, V Nenadovic, J Hutchison**
*Hospital for Sick Children, Toronto, Canada*
*Critical Care* 2005, **9(Suppl 1):**P283 (DOI 10.1186/cc3346)

**Introduction** A prognostic tool is needed in the early assessment of paediatric patients with traumatic brain injury (TBI). The combination of electroencephalography and evoked potentials may help predict outcome.
**Methods** We enrolled patients with TBI admitted to the Paediatric Critical Care Unit with an initial GCS of 12 or less. Patients had an electroencephalogram (EEG), visual evoked potentials (VEPs) and somatosensory evoked potentials (SEPs) done within 60 hours of admission to the PICU, and repeated within 7 days. A CT scan was done on admission. EEG, VEP and SEP were scored. The EEG was analyzed for synchrony using the Hilbert transform. Outcome was measured at 3 months using the Paediatric Cerebral Performance Category Score (PCPC).
**Results** Seven patients aged 3–13 were enrolled. Lowest recorded GSC ranged from 5 to 12. Three of the seven patients developed intracranial hemorrhage. Four of the seven patients sustained diffuse axonal injury; these patients had encephalopathic EEG patterns. Children whose EEG had normal background activity had better outcomes at 3 months. Those who regained normal background activity on the second EEG had intermediate outcomes. Children having the worst scores for EEG and SEP had worst functional outcome. EEG score did not show a correlation with change in the PCPC. Encephalopathic EEGs showed increased synchrony compared with EEGs having a normal background (Fig. 1). Increased SEP latency in cortical to cortical relays correlated with poor functional outcome. SEP score did correlate with change in the PCPC (Pearson coefficient $r = 0.82$, $P = 0.02$). Children whose EEG showed attenuated occipital background patterns had large-amplitude VEPs. Current scoring systems for VEPs do not account for this observed increase.

**Figure 1 (abstract P283)**




Synchrony pattern from EEG electrode C3 of patient 2 in the delta frequency range. Red, maximal synchrony; blue, minimal synchrony. Patient demonstrates synchrony between C3 and between electrodes 1–3, 8–11 and 18. Synchrony is pathological.

**Conclusions** Our results indicate that SEP correlates directly with outcome. EEG synchrony correlates with outcome. High-amplitude VEPs may reflect neuronal hyperexcitability The significance of this needs further investigation.

### P284

### Comparison of biochemical markers and transcranial Doppler ultrasonography findings as early predictors of outcome in patients with traumatic brain injury: preliminary report

**I Rodini[1], A Lavrentieva[1], B Soulountzi[1], C Fitili[2], M Karvouniaris[1], M Bitzani[1]**
*[1]ICU, G Papanikolau Hospital, Theesaloniki, Greece; [2]Microbiology Department, G Papanikolau Hospital, Thessaloniki, Greece*
*Critical Care* 2005, **9(Suppl 1):**P284 (DOI 10.1186/cc3347)

**Introduction** Early brain ischemia after traumatic brain injury (TBI) is predictive of pure outcome. We investigated the time course of biochemical markers of brain damage: serum neuron-specific enolase (NSE) and protein S-100 (Pr S-100) during the first 5 days after the ICU admission. Brain hemodynamics were synchronously assessed using transcranial Doppler ultrasonography (TCD). Each patient was examined with TCD, and the maximum, mean, and the end diastolic velocities and pulsatility index (PI) were evaluated.
**Methods** Eleven patients (aged 34 ± 14.7, APACHE II score 15.7 ± 9, SAPS II 25 ± 13.7) with TBI were included in this prospective study. Paired arterial and jugular bulb blood concentrations of NSE and Pr S-100 were measured daily for five consecutive days and were correlated with neurological outcome evaluated by GOS score. TCD middle cerebral artery velocities and PI were also measured daily after admision and were correlated with biochemical markers and outcome at ICU discharge. The statistical analysis was performed using the Wilcoxon U test and Spearman correlation test.
**Results** NSE and PrS-100 concentrations were significantly higher in patients with poor outcome (GOS 1–3) than in patients with good outcome (GOS 4–5) both in arterial as well as in jugular venous blood samples during the first 5 days. There were significant correlations between these biochemical indicies and the neurological outcome of patients from day 2 after admission (Pr S-100: $r = 0.76$, $P = 0.02$, NSE: $r = 0.67$, $P = 0.03$) that persisted for the following 3 days. TCD findings were not correlated neither with neurological outcome nor with biochemical markers of brain damage.
**Conclusion** The biochemical markers of brain injury (NSE, Pr S=100) seem to be better early outcome prediction parameters than cerebral blood flow velocities and PI measured by TCD in patients with TBI.

### P285

### Clinical progresses and radiological findings in patients with head injury

**K Ishii, K Kitajima**
*Oita University Faculty of Medicine, Oita, Japan*
*Critical Care* 2005, **9(Suppl 1):**P285 (DOI 10.1186/cc3348)

**Purpose** X-ray and computed tomography (CT) are currently the most effective tools in the analysis of head trauma patients. However, the standard for operation of X-ray and CT is still unclear. We investigated the clinical courses and radiological findings in patients with head injury, especially minor trauma.
**Methods** The clinical subjects consisted of consecutive 217 patients, treated by our emergency medicine between January 2003 and December 2004. Among them, Glasgow Coma Scale (GCS) scores in 209 patients (96.3%) were 15. We investigated their clinical courses and radiological findings (X-ray and CT).
**Results** Skull X-ray was performed in 90 patients (41.5%), and CT was performed in 114 patients (52.5%). Skull fracture was shown radiographically in six patients (2.8%), and abnormalities on the initial CT were seen in four patients (1.8%). Two hundred and nine patients with GCS scores of 15 had excellent prognosis except two died. One died because of delayed epidural hematoma, and the other because of crescendo cerebral swelling due to cerebral contusion in the bilateral frontal lobe.
**Conclusions** Head trauma patients must be treated with attention and should undergo X-ray and CT examinations, even in minor injury.

### P286

### The clinical importance of bulbus juguli oxymetry

**C Hoffmann, Z Marjanek, Z Kisvarga**
*Jávorszky Ödön Hospital, Vác, Hungary*
*Critical Care* 2005, **9(Suppl 1):**P286 (DOI 10.1186/cc3349)

**Objective** In our study, we attempted to determine those representative clinical parameters that most exactly correlate with the final outcome of intensive treatment requiring neurological (ischaemic and haemorrhagic stroke) and neurosurgical (subdural and epidural haematoma) cases.
**Methods** We observed 27 patients retrospectively. The cohort was divided into a survivor group I (12 cases) and a non-survivor group II (15 cases). We introduced a central venous canule into the internal jugular vein in the direction of the bulbus juguli, and collected blood samples every 6 hours, at every significant alteration of physical status and at therapeutic intervention. We monitored the cerebral perfusion pressure (CPP) and intracranial pressure (ICP) continously, and measured the oxygen saturation of a blood sample from the bulbus juguli ($SvjO_2$) and the jugular arteriovenous lactate gap every 6 hours, and the GCS every 8 hours. We registrated the change of intracranial structure by computer tomography.
**Results** In group II (non-survivors) the $SvjO_2$ and lactate gap values were 83.83 ± 6.6% and 0.43 ± 0.06 mmol/l, in group I (survivors) the respective values were 71.57 ± 6.26% and 0.2 ± 0.1 mmol/l. We could not find a patient in group II with a GCS higher than 5. There was no significant difference in ICP and CPP values between survivor and non-survivor groups (13.6 ± 2.4 mmHg and 72.3 ± 8.4 mmHg versus 16.4 ± 8.1 mmHg and 68.45 ± 4.6 mmHg).
**Conclusion** The bulbus juguli oxymetry is an invasive but cheap, simple and with competent practical skills a safely applicable monitoring method for the judgement of cerebral oxygenisation. The $SvjO_2$ and lactate gap values were determinative in the aspect of final outcome.

### P287

### Prognostic value of specific neural enolase in head trauma

**C Kaddour, N Baffoun, Z Haddad, M Hamdani**
*National Institute of Neurology, Tunis, Tunisia*
*Critical Care* 2005, **9(Suppl 1):**P287 (DOI 10.1186/cc3350)

**Purpose** Searching for a correlation between the plasma level of specific neural enolase (SNE) and the prognosis of head trauma in the short term.
**Subjects and methods** An open prospective study carried out in a HUC of Tunis over 15 months including 35 patients with head

trauma causing a subarachnoid hemorrhage. Criteria of non-inclusion were age <15 years and 3 months, and head trauma requiring neurosurgery. The management was standardized for all patients to avoid secondary cerebral aggression caused by systemic troubles, as recommended by Maas and colleagues. Clinical basic neurologic survey and CT scan monitoring (Fischer and Marshall classification) were repeatedly carried out. A cerebral CT scan was systematically performed 48 hours after hospitalization or in case of aggravation. A surgical operation was performed throughout the period of the study whenever required (orthopedics, digestive surgery, etc.). The plasma level of SNE was measured on the first, third and fifth day of hospitalization, using the ELISA technique with an immunoenzymatic method, sandwich type (kit CanAg Diagnostics), in a Dias Orin automate (Eti-max 3000). (The normal value of enolase used as a reference in our study was considered the average of 47 volunteers' plasma level.) Statistical analysis used the chi-squared test and variance analysis, respectively, for qualitative and quantitative variables. Values are expressed as means ± standard deviation.

**Results** Mean age: 39 ± 17 years; sex ratio = 4; 80% of patients had a severe head trauma; mortality: 16 patients (45.7%); mean level of SNE in a 'reference population' was 7.02 ± 3.86 μg/ml with a statistically significant difference ($P = 0.001$) (pathologic value above 12.5 μg/ml). Seventeen patients (48.56%) had a pathologic SNE plasma level in the first day. All patients (nine) whose SNE plasma level had still been elevated until the third or the fifth day died. The plasma level was higher in patients who died in comparison with that of surviving patients; 25.74 ± 22.39 μg/ml vs 11.51 ± 4.56 μg/ml, with a significant difference ($P = 0.032$). All dead patients had a higher plasma level of SNE on the fifth day, six of them had a normal value in the first day and then it increased. Patients whose GCS was < 8 had a first-day plasma level so far higher, 24.89 ± 25.27 μg/ml vs 15.25 ± 11.6 μg/ml; but with no significant difference. SNE plasma level was not correlated to the importance of the subarachnoïd hemorrhage (Fischer classification).

**Discussion** The persistence of a high plasma level of specific neural enolase or its elevation represents a short-term prognostic factor. Severe patients have higher plasma levels with no significant difference.

## P288

### S100B protein: a possible prognostic factor in patients with a severe head trauma injury

**P Lavicka, R Pikner, R Bosman, M Choc, I Chytra, O Topolcan**
*Faculty Hospital, Plzen, Czech Republic*
*Critical Care* 2005, **9(Suppl 1):**P288 (DOI 10.1186/cc3351)

**Introduction** S100B protein is a small protein that belongs to the group of calcium binding proteins. It is present in high concentrations in astroglia cells. The level of this marker increases significantly with CNS damage. Normal value is 0–0.2 μg/l.

**Aim** The aim of our research was to evaluate a consequence of a dynamic monitoring of the S100B protein levels for a prognosis of patients with severe head trauma injury.

**Method** Thirty patients with severe head trauma injury were prospectively monitored. All patients were admited to the Emergency Department. The time period from injury to admission was shorter than 6 hours. All patients had the initial CT scan of the brain performed with a positive finding. We used these scoring protocols: at admission GCS, APACHE II, at dismissal GOS, Karnofsky Performance Score (KPS). S100B protein level was done by LIA essay on a fully automated immunoanalyser (Liaison; DiaSorin, Sweden).

**Results** We divided our patients into four groups according to characteristics of the S100B protein levels. The average values of the particular groups are given in Table 1: group A, patients with a rapid decrease of the level; group B, patients with an increasing or persistent high level; group C, patients with a repeated increase of the level after a previous decrease; group D, patients with an initial level above 5 μg/l.

**Table 1**

| Group | Patient Death | number | GCS | APACHE | GOS | KPS | Level 0 | Level 24 | Level 72 |
|---|---|---|---|---|---|---|---|---|---|
| A | 1 | 15 | 9 | 17 | 4 | 80 | 1.378 | 0.415 | 0.245 |
| B | 0 | 5 | 8 | 22 | 3 | 50 | 1.45 | 1.68 | 0.924 |
| C | 2 | 7 | 8 | 26 | 2,5 | 40 | 1.697 | 3.155 | 1.18 |
| D | 3 | 3 | 3 | 37 | 1 | 0 | 18 | – | – |

**Conclusion** A rapid decrease of the level in the first 72 hours is associated with a good prognosis. Increasing or persistent high levels longer than 72 hours are associated with a poor prognosis. A repeated increase level above 1 μg/l after a previous decrease is associated with a poorer outcome. An initial level above 5 μg/l is associated with death.

## P289

### Increased levels of serum S100B protein in critically ill patients without brain injury

**C Routsi, E Stamataki, S Nanas, C Psachoulia, M Zervou, A Koroneos, A Stathopoulos, C Roussos**
*Evangelismos Hospital, Athens, Greece*
*Critical Care* 2005, **9(Suppl 1):**P289 (DOI 10.1186/cc3352)

**Objective** S100B, a calcium-binding protein produced and released predominantly by astrocytes of the central nervous system, has been established as a specific biochemical marker for brain injury [1]. However, there is increasing evidence that S100B release is also induced by other causes or even from tissue outside the brain [2]. The aim of this study was to explore the possible role and the utility of S100B in critically ill patients with respiratory failure of various etiologies, but without brain injury.

**Patients and methods** Thirty-eight mechanically ventilated critically ill patients aged 62 ± 17 years, 29 males, with respiratory and/or organ failure, but with no evidence of brain injury or other neurological disorder, were prospectively studied. Blood samples for analysis of serum S100B protein were obtained from the radial artery at the time of laboratory sampling and blood gas analysis. For the determination of S100B, all samples were analyzed using a commercially available immunoluminometric assay (LIASON; Sangtec Medical, Bromma, Sweden). Blood gases and lactate were analyzed using the ABL 625 analyzer (Radiometer Copenhagen, Denmark) and then the arterial oxygen content was calculated.

**Results** Serum S100B was measured in 16 medical and 22 surgical ICU patients with a SOFA score on admission of 8 ± 3.4. Compared with the normal values (< 0.15 μg/l), almost all patients exhibited increased serum S100B levels at least once (0.56 ± 1.03 μg/l, mean ± standard deviation, range 0.04–9.25). Pearson's correlation showed a statistically significant relation between S100B and Hb ($P < 0.001$), $O_2$ content ($P = 0.002$), and arterial lactate ($P < 0.001$). Multivariate analysis using a stepwise logistic regression model showed that the lactate was an independent variable ($F = 9.6$, $P < 0.001$), followed by $O_2$ content ($F = -3.25$, $P = 0.02$).

**Conclusions** Serum levels of S100B protein are elevated in critically ill patients and correlate with increased lactate levels, low hemoglobin, and abnormal oxygen content. Further research should determine the sources of this S100B release and evaluate its significance as a possible marker of tissue hypoperfusion in the ICU setting.

**References**

1. *Br J Neurosurgery* 1999, **13:**56.
2. *Neurosurgery* 2001, **48:**1255.

**P290**

## S100B protein in heroin overdose: a pilot study

**M Brvar, J Ambrozic, J Osredkar, M Mozina, M Bunc**
*University Medical Center Ljubljana, Slovenia*
*Critical Care* 2005, **9(Suppl 1):**P290 (DOI 10.1186/cc3353)

**Objective** Heroin overdose could result in hypoxic-ischemic changes with cerebral edema, ishemic neuronal damage and neuronal loss due to central nervous depression with significant respiratory depression and hypotension. Heroin overdose can cause cognitive impairment, neurological deficits or even death. S100B, the structural protein of astroglia, has already been shown to be a useful neurobiochemical marker of brain damage in circulatory arrest, stroke, traumatic head injury and carbon monoxide poisoning. The aim of our study was to assess the possible role of S100B as a biochemical marker of brain injury in heroin overdose.

**Methods** The prospective study included patients with heroin overdose who were admitted to the Emergency Department (ED). Patients were enrolled if they had a documented exposure to heroin only. The physical and neurological examinations were carried out on the scene and on arrival at the ED. Neuropsychological testing was performed at the ED just before the patient's discharge. Blood samples for S100B determination were drawn immediately after arrival at the ED. S100B concentrations were measured with a commercial immuno-luminometric assay. Blood samples were also analyzed for creatine kinase, troponin I and creatinine level. A toxicology analysis of patient's blood or urine samples by gas chromatography coupled to mass spectrometry was performed. The control group included 10 healthy volunteers. Data are presented as the mean. S100 levels between groups were compared using the Mann–Whitney U test and the Pearson correlation coefficients were calculated for S100B, creatine kinase, troponine I and creatinine levels. A $P$ value of less than 0.05 was considered significant.

**Results** A total of 20 patients with heroin overdose were enrolled. The mean age of the study cohort was 24.5 years (range, 16–39 years). There were four women and 16 men. Heroin overdose was unintentional in all patients. All patients were unconscious on the scene and regained conciseness after naloxone application. 6-Monoacetyl-morphine, a metabolite of heroin, was detected in all patients. S100B levels of heroin overdosed patients were significantly higher compared with S100B levels of the control group (0.65 μg/l vs 0.07 μg/l, $P < 0.05$). Twelve patients (60%) had elevated creatine kinase with mean value 15.30 μkat/l (normal value 0.17–2.08 μkat/l) indicating rhabdomyolysis and two (10%) of them also had elevated troponine I (0.15 and 0.1 μg/l; normal value 0.06 μg/l) indicating myocardial necrosis. No correlation was found between serum S100B, creatine kinase, troponine I and creatinine levels ($P > 0.05$). All patients survived and had no clinically detectable neurological deficits on discharge. Psychological testing was unsuccessful because the majority of patients refused testing.

**Conclusion** Heroin overdose is associated with elevated S100B levels. S100B could be useful biochemical marker of heroin overdose, but its clinical value to predict brain tissue damage with neurological or cognitive deficits after heroin overdose should be further evaluated.

**P291**

## Paired serum S-100B and neuron-specific enolase assay in early and fast assessment of brain damage after cardiac arrest

**C Crippa, G Larosa, R Dorizzi, A Merlini, E Pecci, E Polati, A Luzzani**
*Institute of Anesthesiology & Intensive Care, Verona, Italy*
*Critical Care* 2005, **9(Suppl 1):**P291 (DOI 10.1186/cc3354)

**Background and purpose** Early and accurate predictors of neurological outcome in patients with hypoxic-ischemic encephalopathy after cardiac arrest are needed in order to improve medical decision-making. The aims of the present study were: to assess serum S-100 protein and neuron-specific enolase (NSE) as early markers of brain damage and outcome after cardiac arrest; and to compare the diagnostic and prognostic power of these serum markers to somatosensory evoked potentials (SSEP).

**Design** A prospective study. Clinicians were blinded to S-100 and NSE results.

**Setting** The ICU of a university hospital.

**Methods** Twenty-five patients resuscitated from cardiac arrest (CA) were assessed until they regained consciousness or until death/permanent vegetative state. We correlated SSEP, S-100 protein and NSE serum concentrations with patient outcome. S-100 protein and NSE serum concentrations were measured using an automated chemiluminescent analyzer (Liaison; Diasorin, Saluggia, Italy) in samples collected 24, 48, 72 and 168 hours after the cardiopulmonary resuscitation (CPR); SSEP were recorded at 48 hours and on day 7 after the CPR.

**Results** We enrolled 25 consecutive patients (17 males/eight females, mean age 69 ± 17 years, mean APACHE II score 26 ± 4.5); eight of them regained consciousness. Median values of NSE and S-100B serum concentrations were significantly (Mann–Whitney U test) higher in patients who did not regain consciousness compared with patients who regained consciousness at all time intervals (NSE: 53 vs 24 μg/l at 24 hours; 137 vs 20 μg/l at 48 hours; 102 vs 16 μg/l at 72 hours, and 39 vs 6 μg/l 168 hours after CA; S-100B: 2882 vs 342.5 ng/l at 24 hours; 6514 vs 240 ng/l at 48 hours; 3125 vs 198 ng/l at 72 hours, and 610 vs 146 ng/L 168 hours after CA).

S-100B concentration cut-off of 776 ng/l at 24 hours was found the best predictor of not regaining consciousness. The area under the curve was 0.96 (95% confidence interval = 0.88–1.00); specificity was 100%; sensitivity was 82.4%. NSE concentration cut-off point of 45 μg/l at 48 hours was found the best predictor of not regaining consciousness. The area under the curve was 0.87 (95% confidence interval = 0.72–1.00); specificity was 100%; sensitivity was 81.2%.

High association between SSEP responses and outcome was found at 48 hours (rho = 0.68, $P < 0.001$) and at 7 days (rho = 0.72, $P < 0.001$) (Spearman correlation).

**Conclusions** According to our study and previous reports [1,2] biochemical markers, and especially S100 protein, provide reliable information about patient outcome after acute global cerebral ischemia. Moreover, we used a recently marketed analyzer that makes available S-100 protein and NSE results within 1 hour; in this way, clinicians can easily and promptly use them in the management of the patient.

**References**

1. Hachimi-Idrissi S, Van der Auwera M, Schiettecatte J, *et al.*: *Resuscitation* 2002, **53:**251-257.
2. Martens P, Raabe A, Johnsson P: *Stroke* 1998, **29:**2363-2366.

## P292

### Neuron-specific enolase level predicts survival of patients after cardiopulmonary resuscitation

**J Auer, R Berent, G Lamm, T Weber, M Porodko, C Punzengruber, E Maurer, B Eber**
*General Hospital Wels, Austria*
*Critical Care* 2005, **9(Suppl 1):**P292 (DOI 10.1186/cc3355)

**Background** The prediction of outcome in patients after prolonged cardiopulmonary resuscitation (CPR) has enormous ethical and socioeconomic implications. The present study investigated the prognostic relevance of the early time course of serum neuron-specific enolase (NSE) as a biochemical marker of ischemic brain injury in individuals after CPR.
**Methods and results** NSE levels were assessed immediately after restoration of spontaneous circulation (ROSC), 6 hours, 12 hours, and 2 days following prolonged CPR from nontraumatic, normothermic, inhospital or out-of-hospital cardiac arrest in eight male and 12 female patients. The survival status was assessed during the entire hospital stay.
NSE levels in survivors and nonsurvivors immediately after ROSC, 6 hours, 12 hours, and 48 hours after following prolonged CPR were 18.8 ± 13.8 μg/l, 18 ± 7.9 μg/l, 17.9 ± 10.1 μg/l, 14.4 ± 7.1 μg/l, and 26.5 ± 15 μg/l, 49.3 ± 65.5 μg/l, 60.8 ± 72 μg/l, 86.5 ± 87.6 μg/l, respectively. Nonsurvivors had significantly higher NSE levels 48 hours after ROSC than survivors ($P = 0.03$) and showed a strong trend towards higher values during the entire time course following CPR. NSE concentrations at 48 hours after ROSC of > 23 μg/l and > 29.5 μg/l predicted death with a high specificity (95% and 100%, respectively). In contrast, NSE levels of 15 μg/l or less at 48 hours predicted survival with a high specificity (100%).

**Table 1**

| | Normal value | Baseline | 6 hours | 12 hours | 48 hours |
|---|---|---|---|---|---|
| NSE, survivors (μg/l) | 3–14 | 18.8 ± 13.8 | 18 ± 7.9 | 17.9 ± 10.1 | 14.4 ± 7.1 |
| NSE, nonsurvivors (μg/l) | 3–14 | 26.5 ± 15 | 49.3 ± 65.5 | 60.8 ± 72 | 86.5 ± 87.6 |
| *P* value | – | 0.23 | 0.2 | 0.11 | 0.03 |

**Conclusion** Serum NSE levels early after ROSC are valuable additional parameters for the prediction of outcome in patients after prolonged CPR.

## P293

### Retrograde cerebral perfusion of oxygenated compacted red blood cells attenuate the brain damage after hypothermia circulation arrest of rat

**DS Su, XR Wang, YJ Zheng, YH Zhao, TJ Zhang**
*Institute of Anesthesiology, Renji Hospital, Shanghai Second Medical University, Shanghai, China*
*Critical Care* 2005, **9(Suppl 1):**P293 (DOI 10.1186/cc3356)

**Background** It was proved that higher haematocrit (Hct) might improve the function of brain after hypothermia circulation arrest (HCA). In the present study we develop a new rat HCA model and investigate whether retrograde cerebral perfusion of oxygenated compacted red blood cells (RBC) could attenuate the brain injury after HCA.
**Methods** A new rat HCA model was developed. Forty-eight rats were randomly distributed into three groups: HCA alone group, HCA combined with retrograde perfusion oxygenated compacted red blood cell group (HCArcp group), and sham operation group (sham op group); 16 rats in each group. All experimental group animals underwent HCA for 90 min at 18°C. We evaluated the brain injury after HCA with the light microscopy and electron microscopy. By the immunohistochemistry and RT-PCR techniques we measured the different expression of the C-Fos, Bcl-2, Bax mRNA and protein between groups. Additionally we measured the wet/dry ratio of the brain in order to evaluate the edema degree after HCA.
**Results** The new HCA model of the rat we developed was comparable with the clinical setting not only in terms of the intubation and anesthesia method and materials employed, but also in terms of the priming capacity in relation to body weight. The numbers of degeneration and necrosis neurons in the hippocampus CA1 and parietal cortex but not in the thalamus of the HCA alone group were significantly greater than those of the HCArcp group ($P < 0.05$). The mean score of mitochondrion of the hippocampus CA1 in the HCA alone group was significantly higher than that of the HCArcp group ($P < 0.05$). The expression of C-Fos, Bax mRNA and protein in hippocampus CA1 and/or parietal cortex area was higher in the HCA alone group than that of the HCArcp group ($P < 0.05$). Expression of the mRNA and protein of Bcl-2 was higher in the HCArcp group than that of the HCA alone group ($P < 0.05$). The degree of edema after HCA between the two experiment groups had no significant difference ($P > 0.05$).
**Conclusion** We made a new rat model of HCA comparable with the clinical setting. Retrograde cerebral perfusion of oxygenated compacted RBC is a safe and effective method to protect the brain during HCA. Adjusting the gene expression related with apoptosis might contribute to the neuroprotective effects of retrograde oxygenated compacted RBC.

## P294

### A prospective single-center pilot study to evaluate the feasibility and the safety of venovenous cooling to induce mild hypothermia after cardiac arrest

**D Rubes, M Matias, J Rulisek, M Lips, E Poliachova, I Vykydal, Z Stach, J Kunstyr, T Kotulak, M Stritesky**
*Prague General University Hospital, Prague, Czech Republic*
*Critical Care* 2005, **9(Suppl 1):**P294 (DOI 10.1186/cc3357)

**Background** Mild poresuscitative hypothermia improves neurologic outcome after cardiac arrest. Animal studies indicate that rapid induction of the target temperature may be even more neuroprotecive. Currently available methods allow only slow induction of hypothermia (less than 1°C/hour). A faster cooling method could reduce neurologic morbidity and mortality.
**Methods** We evaluated safety and feasibility of venovenous extracorporal cooling to induce mild hypothermia in a prospective non-randomised single-center clinical study. Eleven patients with witnessed out-of-hospital or inhospital cardiac arrest who remained comatose after the restoration of spontaneous circulation were treated with hypothermia induced with venovenous extracorporal cooling via a double lumen catheter inserted into the v. femoralis. After the induction phase, hypothermia was maintained at 32–34°C for 24 hours with a cooling mattress. The rewarming phase lasted 12 hours. Primary endpoints were the time to reach the target temperature (34°C) and the rate of complications in first 7 days.
**Results** Eleven patients were enrolled, age 19–78 years, seven males. Average time to reach a temperature of 34°C was 75 min (range 55–118 min, 95% confidence interval 63–86.5). Cooling averaged 1.97°C/hour (range 1.57–2.58°C/hour, 95% confidence

interval 1.76–18°C). No procedure-releated adverse events occured. Four patients (36%) had Glasgow Outcome scale 1–2 14 days after the cardiac arrest.

**Conclusion** Extracorporeal venovenous cooling is a safe and fast method for induction of mild hypothermia in patients who underwent cardiac arrest. To prove the hypothesis that the faster the induction of hypothermia the better neurologic outcome, a much larger study is needed.

### P295

### Therapeutic hypothermia post cardiac arrest: an evidence-based guideline

**O Al-Muslim[1], K Burns[2], C Martin[2]**
*[1]Riyadh Armed Forces Hospital, Riyadh, Saudi Arabia;*
*[2]The London Health Sciences Centre, London, Canada*
*Critical Care* 2005, **9(Suppl 1):**P295 (DOI 10.1186/cc3358)

**Introduction** Recent studies have shown that induced hypothermia improves neurologic outcome in comatose survivors of cardiac arrest (CA). Our goal was to develop, implement and evaluate an evidence-based guideline for the management of comatose survivors of cardiac arrest.

**Methods** A systematic review of the literature was conducted to identify potentially relevant randomized clinical trials and observational studies reporting on a strategy of therapeutic hypothermia in comatose survivors of out-of-hospital CA. The research design and methodologic quality of all studies meeting our inclusion criteria were evaluated independently and in duplicate.

**Results** Three randomized clinical trials (RCTs) and six observational studies were evaluated. Pooling the RCT data of good neurologic outcome showed an odds ratio of 2.06 (95% confidence interval 1.34–3.15; $P = 0.001$) favoring therapeutic hypothermia strategy. Two RCTs support the use of a hypothermia strategy for the management of patients with witnessed CA due to ventricular fibrillation while one small RCT supports its use in patients with pulseless electrical activity or asystole. Although most studies used external cooling measures to induce and maintain mild hypothermia (32–34°C), one study used a 30 ml/kg bolus of cold (4°C) crystalloid during the induction of hypothermia. Duration of cooling ranged from few hours to about 3 days. Cointerventions in the evaluated studies were anesthetic agents, hemodynamic support, mechanical ventilation, glucose management and treatment of acute coronary syndrome. The evaluated trials were used to develop a practice guideline. The guideline was implemented during a pilot study to assess its feasibility. During this pilot phase, 16 patients were treated. The patients' characteristics and their outcomes data were comparable with the results of the clinical trials.

**Conclusion** An evidence-based guideline for the management of comatose survivors of cardiac arrest is helpful to disseminate the strategy of induced hypothermia into clinical practice.

### P296

### Therapeutic hypothermia: pitfalls and pearls

**M Busch, E Søreide**
*Rogaland Central Hospital, Stavanger, Norway*
*Critical Care* 2005, **9(Suppl 1):**P296 (DOI 10.1186/cc3359)

**Background and goal** Mild therapeutic hypothermia (MH) improves neurological recovery after prehospital cardiac arrest (OHCA) [1] and has become a standard procedure in post-resuscitative care. Our goal was to study the complications during MIH [2].

**Materials and methods** We evaluated retrospectively 30 patients after VF-OHCA with regard to complications associated with the use of MIH. MIH was induced by use of a surface cooling protocol and maintained for 12–24 hours. Incidence of koagulopathy, electrolyte disorders, pneumonia (within 72 hours after admission), leukopenia, pancreatitis, hemorrhage, elevated amylase and arrhythmias requiring treatment were documented.

**Results and discussion** The median age of the patients was 60.5 years (32–75 years), with all patients (100%) having presumed cardiac cause of OHCA and ventricular fibrillation/pulsless ventricular tachykardia (VF/VT) as the initial ECG rhythm. All patients were intubated at the scene. The presenting arrhythmias during MIH were VF in one patient, VT in two patients and rapid atrial fibrillation in four patients.

**Table 1**

| Complication | Incidence (%) |
|---|---|
| Hypokalemia | 73 ($n = 22$) |
| Severe hypokalemia (< 3.1 mmol/l) | 36.6 ($n = 11$) |
| Pneumonia | 70 ($n = 21$) |
| Elevated amylase | 53.3 ($n = 16$) |
| Arrhythmia | 23.3 ($n = 7$) |
| Hyperkalemia during rewarming | 3.33 ($n = 1$) |
| Elevated INR (1.3–1.6) | 16.6 ($n = 5$) |
| Platelet reduction > 30% | 10 ($n = 3$) |
| Insulin resistance | 16.6 (n = 5) |
| Leukopenia | 0 |
| Thrombocytopenia | 0 |
| Pancreatitis | 0 |
| Hemorrhage | 0 |

**Conclusion** MIH is a safe therapy when the clinician is aware of the potential side effects. Electrolyte disorders during MIH and pneumonia after MIH treatment should be anticipated and treated pre-emptively.

**References**

1. Nolan J: *Resuscitation* 2003, **57:**231-235.
2. Polderman KH: *Int Care Med* 2004, **30:**757-769.

### P297

### The European Resuscitation Council Hypothermia After Cardiac Arrest Registry: presentation and plans

**J Arrich**
*Medical University Vienna, Austria*
*Critical Care* 2005, **9(Suppl 1):**P297 (DOI 10.1186/cc3360)

**Introduction** Resuscitative hypothermia after cardiac arrest has been shown to improve neurological outcome and has been added to the recommendations for the treatment of cardiac arrest patients of the Task Force of the International Liaison Committee on Resuscitation [1–3]. However, there is clearly a need for further investigations. A population-based international database, the European Resuscitation Council (ERC) Hypothermia After Cardiac Arrest Registry (HACA-R), is on its way to provide sufficient data to answer relevant study questions (see www.erchacar.org, www.erc.edu). It was established in 2002 under the lead of the ERC. The goals of the HACA-R are: to document information of all patients with cardiac arrest admitted to one of the participating centres; to set up relevant study protocols in close collaboration with the clinicians of the ERC to further improve guidelines on

application of mild therapeutic hypothermia; and to formulate hypothesis on underlying causes of the benefits of mild therapeutic hypothermia on neurological outcome of cardiac arrest patients.

**Methods** Protocols on baseline characteristics, details on cardiac arrest, out-of-hospital procedures and events, cooling and rewarming procedures, neurological and functional outcome scores at discharge, information on possible adverse events and death are documented.

**Results** From March 2003 to May 2004, 301 patients across 16 sites have been enrolled. Of all enrolled patients 93 (31%) received endovascular cooling, 30 (10%) were cooled with other methods, 178 (52%) acted as control, 75 (25%) were female, the mean age was 60 (STD 15) years. A detailed analysis will be conducted when a sufficient set of patient data has been completed.

**Conclusion** With the effort of a growing number of participating centres, the ERC HACA-R is expected to become a useful tool to further elucidate scientific questions regarding resuscitative hypothermia after cardiac arrest and to realize goals of the ERC.

**References**

1. Bernard SA, Gray TW, Buist MD, Jones BM, Silvester W, Gutteridge G, Smith K: **Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia.** *N Engl J Med* 2002, **346:**557-563.
2. HACA authors: **Mild therapeutic hypothermia to improve the neurological outcome after cardiac arrest.** *N Engl J Med* 2002, **346:**549-556.
3. Nolan JP, Morley PT, Vanden Hoek TL, Hickey RW: **Therapeutic hypothermia after cardiac arrest.** *Resuscitation* 2003, **57:**231-235.

## P298

## Hypothermia in a surgical intensive care unit

**F Abelha, N Landeiro, A Neves, C Santos, M Castro**
*Hospital de São João, Porto, Portugal*
*Critical Care* 2005, **9(Suppl 1):**P298 (DOI 10.1186/cc3361)

**Background and goal** Inadvertent hypothermia is not uncommon in the immediate postoperative period and it is associated with impairment and abnormalities in various organs and systems that can lead to adverse outcomes. The aim of this study was to estimate the incidence, predictive factors and outcome of core hypothermia at admission to a surgical ICU.

**Materials and methods** All 185 adult patients who underwent scheduled or emergency noncardiac surgery admitted to a surgical ICU between April and July 2004. The tympanic membrane core temperature (Tc) was measured on arrival on the ICU and every 2 hours until 6 hours after admission. The following variables were also recorded: age, sex, body weight and height, preoperative body temperature, ASA physical status, emergency or scheduled surgery, magnitude of surgical procedure, anesthesia technique, amount of fluids during anesthesia, use of temperature monitoring and warming techniques, duration of the anesthesia, length of stay in the ICU and in the hospital, and SAPS II score. The incidence of core hypothermia at admission to the ICU and its 95% confidence interval (CI) were calculated using the cutoff point of Tc < 35.0°C. That was used to classify patients as either hypothermic or normothermic. The two groups were compared to assess the relationship between each clinical predictor and core hypothermia using univariate analysis performed by simple binary logistic regression with an odds ratio (OR) and its 95% CI.

**Results** The mean (± standard deviation) admission Tc was 34.69 ± 1.02°C. Incidence of core hypothermia on ICU admission was 57.84%. Temperature monitoring (OR 0.185, 95% CI 0.053–0.651, $P = 0.009$), use of warming techniques (OR 0.473, 95% CI 0.258–0.865, $P = 0.015$) and higher previous body temperature (OR 0.402, 95% CI 0.206–0.784, $P = 0.007$) were significant protective factors against core hypothermia.

Significant independent predictors of hypothermia at admission were the magnitude of surgery (OR 3.110, 95% CI 1.235–7.831, $P = 0.016$ for medium surgery; OR 4.679, 95% CI 2.063–10.613, $P < 0.001$ for major surgery), use of general anesthesia or combined epidural and general anesthesia (OR 5.963, 95% CI, 1.891–18.804, $P = 0.002$ for general anesthesia; OR 22.50, 95% CI 2.068–244.838, $P = 0.011$ for combined epidural and general anesthesia), amount of crystalloids (OR 1.435, 95% CI 1.161–1.773, $P = 0.001$) and total blood administration (OR 1.575, 95% CI 1.142–2.170, $P = 0.006$), anesthesia longer than 3 hours (OR, 1.808; 95% CI, 1.002–3.263, $P = 0.049$) and SAPS II scores (OR 1.028, 95% CI 1.004–1.052, $P = 0.020$). Twenty-nine patients (15.70%) died during their hospitalization. Hypothermia was not a risk factor for mortality, not at admission, neither at 2, 4 and 6 hours after arrival on ICU. Statistically significant independent risk factors for mortality were low body weight (OR 0.970, 95% CI 0.941–0.999, $P = 0.044$) and low body mass index (OR 0.895, 95% CI 0.815–0.982, $P = 0.019$), emergency surgery (OR 7.109, 95% CI 2.902–17.419, $P < 0.001$), major surgery (OR 5.500, 95% CI 1.133–26.690, $P = 0.034$), high SAPS II scores (OR 1.105, 95% CI 1.067–1.144, $P < 0.001$), longer stay in ICU (OR 8.686, 95% CI 3.646–20.692, $P < 0.001$ for length of stay longer than 2 days) and in the hospital (OR 1.024 per day, 95% CI 1.011–1.038, $P < 0.001$).

**Conclusions** The incidence of patient hypothermia on arrival in intensive care is very high but is not an independent factor for mortality or for staying longer in the ICU. All efforts should be made for preventing hypothermia that should include temperature monitoring and more often use of methods of warming patients and intravascular fluids.

## P299

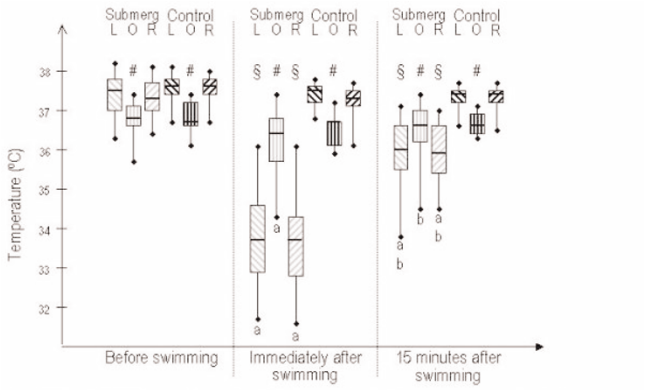
## Infrared ear thermometry in drowning: not a good choice

**U Ehrmann[1], E Shank[2], B Hauser[1], M Gröger[1], P Radermacher[1], C Muth[1]**
*[1]University of Ulm, Germany; [2]Massachusetts General Hospital, Boston, MA, USA*
*Critical Care* 2005, **9(Suppl 1):**P299 (DOI 10.1186/cc3362)

**Introduction** Hypothermia is a serious problem in many out-of-hospital emergencies [1], one of them being (near-)drowning. Hypothermia *per se* may threaten the patient, but it can also protect vital organs [1,2]. Since severe hypothermia also impacts the decision where to bring the victim for further treatment [2], exact temperature measurement assumes crucial importance in this context. The purpose of this trial was to determine the reliability of the tympanic temperature measurement after immersion in water.

**Materials and methods** The trial was approved by the ethics committee of the University of Ulm. In 28 volunteers aged 18–49 years sublingual (Fixotherm; Tradesell Europe, Eglharting, Germany) and tympanal (First Temp Genius; Sherwood Medical, Sulzbach, Germany) temperature measurements were taken before immersion in water, immediately after the 45 min of immersion, and 15 min after leaving the water. We measured the oral temperature once at each of these three time-points. During immersion the volunteers had to swim in a manner that provides a temporary submersion of the ears. The control group consisted of 11 volunteers who had to swim for the same time with their heads always above the water. The trial was performed in an indoor swimming pool at 28°C water temperature and 30°C air temperature.

**Figure 1 (abstract P299)**




Right (R) and left (L) tympanic, and oral (O) temperature in the submerged and control groups. Data are median (quartiles, range). § tympanic temperature significantly different (p<0.01) vs. controls, # oral temperature significantly different (p<0.01) vs. tympanic temperature, a,b significantly different (p<0.01) vs. before swimming (a) or immediately after swimming (b).

**Results** In both groups oral temperature time-dependently varied within only 0.4°C. Tympanic temperature was significantly lower after immersion compared with the baseline values in the 'submerged' group (Submerg) (33.7 vs 37.5°C, $P < 0.001$), while no such effect was observed in the control subjects (37.6 vs 37.5°C, $P = 0.31$). At baseline, oral temperature was lower than tympanic temperature in both groups ($P < 0.001$), while this relation was reversed after immersion. This reversed response was not detectable in the controls.

**Conclusions** The data suggest that in emergencies like near-drowning, the use of infrared ear thermometry to measure body (core) temperature should be cautioned.

**References**

1. Giesbrecht: *Aviat Space Environ Med* 2000, **71:**733.
2. Wollenek G, *et al.*: *Resuscitation* 2002, **52:**255.

## P300

### Is there any relation between hypothermia and outcome in critically ill patients?

**F Bozorgi[1], M Abbasi[2], M Zare[2], A Arhamidolatabadi[1], A Hosseinnejad[2], D Farsi[2]**
*[1]Beheshti University of Medical Sciences, Tehran, Iran; [2]Iran University of Medical Sciences, Tehran, Iran*
*Critical Care* 2005, **9(Suppl 1):**P300 (DOI 10.1186/cc3363)

Hypothermia is defined as a core temperature less than 35°C, which is commonly seen in patients with loss of consciousness and trauma. It increases the mortality and morbidity due to impaired cardiorespiratory function, peripheral vasoconstriction, bleeding diathesis, metabolic acidosis, diminished hepatorenal function and impaired immune response. We decided to investigate the prevalence of hypothermia and its relationship with patient outcome considering the problems mentioned and inadequate attention to hypothermia.

This investigation was performed in 100 emergent patients who presented to the ED of Rasol Akram Hospital. This discriptive study was carried out during 4 months. We used a tympanic infrared thermometer for patient detection upon arrival. Data were analyzed by a statistical method (Student *t* test, chi-square test), and the goal was to find the relation between patient core temperature and their outcomes in emergent patients. Some other data such as mortality and the need for critical care or ward admission were also included.

Based on this study, hypothermia was detected in 35.3% of patients. There was a significant correlation between hypothermia and mortality ($P < 0.002$).

Hypothermia was more prevalent in patients who were died but there was no significant correlation between hypothermia and the need for critical care length of stay, although there was minimal difference with normothermic patients.

## P301

### Influence of cardiopulmonary resuscitation on levels of tumor markers

**J Auer, R Berent, G Lamm, M Porodko, C Punzengruber, T Weber, G Aspöck, B Eber**
*General Hospital Wels, Austria*
*Critical Care* 2005, **9(Suppl 1):**P301 (DOI 10.1186/cc3364)

**Background** Tumor markers (TM) including alpha-fetoprotein (AFP), carcinoembryonic antigen (CEA), CA 15-3, and prostate-specific antigen (PSA) are serum markers for malignant diseases. Previous studies investigating the effect of acute and chronic inflammation, cardiopulmonary bypass surgery, and cardio-pulmonary resuscitation (CPR) on levels of TM showed conflicting results. CPR may result in a profound inflammatory response and is frequently associated with severe tissue hypoperfusion. The present study investigated whether AFP, CEA, CA 15-3, and PSA are influenced by CPR.

**Methods and results** AFP, CEA, CA 15-3, and PSA (only in male patients) were assessed immediately after hospital admission, 6 hours, 12 hours, and 2 days after prolonged CPR in eight male and 12 female patients. Serum levels of AFP, CEA, CA 15-3 did not change significantly after CPR. PSA levels increased significantly with a peak 48 hours after CPR ($3.3 \pm 3.1$ and $28.3 \pm 30.5$ ng/ml for baseline and 48 hours levels, respectively; $P < 0.001$). AFP, CEA, CA 15-3, and PSA (in males) values above the normal range were observed in 0%, 13.8%, 3.8%, and 46.9% of all measurements, respectively. At least one value above the

**Table 1 (abstract P301)**

**Mean (± standard deviation) serum levels of AFP, CEA, CA 15-3, and PSA**

| | Normal values | Baseline | 6 hours | 12 hours | 48 hours |
|---|---|---|---|---|---|
| AFP (ng/ml) | 0 – 15 | 3.2 ± 2.4 | 3.1 ± 2.4 | 6.2 ± 8.0 | 3.0 ± 2.5 |
| CEA (ng/ml) | 0 – 5 | 3.7 ± 3.5 | 3.7 ± 3.2 | 3.6 ± 3.0 | 3.6 ± 3.1 |
| CA 15-3 (U/ml) | 0–35 | 19.4 ± 9.7 | 18.7 ± 9.4 | 3.6 ± 3.0 | 16.5 ± 8.8 |
| PSA (ng/ml) | ≤ 70 years < 4.5<br>> 70 years < 6.5 | 3.3 ± 3.1 | 6.2 ± 8.0 | 16.8 ± 25.0 | 28.3 ± 30.5 |

normal range was observed in 0%, 20%, 5%, and 75% of all patients for AFP, CEA, CA 15-3, and PSA (in males), respectively. Baseline values of AFP, CEA, CA 15-3, and PSA (in males) were above the normal range in 0%, 15%, 5%, and 10% of all patients, respectively. Levels for all markers did not differ significantly between survivors and nonsurvivors.
**Conclusions** Prolonged CPR does not influence AFP, CEA, CA 15-3 serum levels, but is frequently associated with increases of PSA. Thus, in contrast to PSA, interpretation of AFP, CEA, CA 15-3 serum levels is not influenced by recent CPR.

### P302

### Descriptive analysis of contributing factors in outcomes of emergency department CPRs

**A Arhami Dolatabadi[1], A Setayesh[2], M Zare[2], A Hosseinnejad[2], F Bozorgi[1], D Farsi[2]**
*[1]Beheshti University of Medical Sciences, Tehran, Iran; [2]Iran University of Medical Sciences, Tehran, Iran*
*Critical Care* 2005, **9(Suppl 1):**P302 (DOI 10.1186/cc3365)

**Introduction** CPR can avoid 25% of deaths especially out-of-hospital cases. Cases of cardiac arrest are usually studied from epidemiological aspects. This study is designed to guide us through our Emergency Department (ED) and EMS managements.
**Methods and materials** In this observational cross-sectional study, 195 patients admitted to the ED of Rasoul Akram hospital during 11 month from June 2003 to April 2004 were included. Age, sex, time, place, cause and witness of arrest, BLS/ALS, out-of-hospital intubations, transportation vehicle, CPR outcome and final status of patients were gathered in a data registration form.
**Results** The mean (± standard error of the mean) age was 59.33 ± 1.4, there was a significant difference in mean age between males and females ($P = 0.003$). A total 41.5% of cases arrested in the ED, 14.9% had no witness, 56.4% were transported to hospital by ambulance, 53.3% received no life support before arrival and 13.3% had been intubated out of hospital. The first rhythm checked in the ED was asystole in 73.3%. Cardiovascular problems constituted 42.1% of causes. There was a significant difference in cause of cardiac arrest between age groups ($P = 0.000$). A total 59.5% of CPRs were successful; there was no significant difference in sex ($P = 0.199$) and age ($P = 0.746$) groups and different cause categories. CO poisoning and hanging had maximal mortality (100%). Age, sex distribution ($P = 0.07$), time of cardiac arrest, place of collapse ($P = 0.1$), cause of arrest, being witnessed, performed BLS/ALS ($P = 0.7$), intubations ($P = 0.76$), initial cardiac rhythm, and transportation vehicle had no effects on patients final status. CPR outcome ($P = 0.000$) and the cause of arrest ($P = 0.000$) affected the final status of patients. Finally, 93.3% of patients expired and 6.7% of patients were discharged from hospital.
**Discussion** Successful CPR was performed in the majority of cases. But the overall prognosis was poor. The main determining factor of final status was the cause of arrest.

### P303

### Identification of agonal breathing by dispatchers to improve the detection and treatment of cardiac arrest

**L Roppolo, P Pepe, A Westfall, A Idris, J Wigginton**
*University of Texas Southwestern Medical Center and the Parkland Health and Hospital System, Dallas, TX, USA*
*Critical Care* 2005, **9(Suppl 1):**P303 (DOI 10.1186/cc3366)

**Background** In as many as 40% of applicable out-of-hospital cardiac arrest (OOHCA) cases, bystanders do not receive instructions over the telephone from public safety dispatchers to perform cardiopulmonary resuscitation (CPR) because the bystanders report that the patient is 'breathing' due to the presence of agonal respirations.
**Objective** To determine whether a new dispatcher assessment protocol could better identify agonal breathing and thus more cases of OOHCA that might benefit from CPR instructions.
**Methods** Study of all dispatcher-assisted OOHCA cases in a large municipality (population 1.2 million) for the 8 months before and 4 months after protocol implementation (November 2003). In the protocol, the call-taker asks about gasping defined as either 'slow, barely breathing' or 'slow, noisey/gurgling'. If unsure, the caller places the telephone near the patient's mouth and the dispatcher listens for breathing, or the bystander is asked to state each time the patient takes a breath.
**Results** Among 962 consecutive patients identified as having OOHCA (57% male, 43% female; mean age 63 ± 17 years, range 17–106), the presenting rhythm was ventricular fibrillation or pulseless electrical activity in 85% of those identified with agonal breaths versus 46% without them ($P = 0.002$) and such presentations had a higher rate of survival to hospital admission ($P < 0.0001$). After protocol introduction, the percentage of OOHCA patients thought to be 'breathing' normally fell from 28% (168/599) to 19% (68/362; $P = 0.0012$). Also, in the 8 months before the protocol, no patient had their agonal respirations detected compared with 22 patients detected in the 4 months afterwards ($P < 0.0001$). No adverse problems were reported from the subsequent performance of CPR in these agonal breathing cases.
**Conclusion** Introduction of a supplemental dispatcher assessment protocol (that includes questioning about agonal respirations) can significantly increase cardiac arrest detection over the telephone, thus increasing the opportunity for dispatchers to provide CPR instructions for those very patients who, in fact, may a higher propensity for survival than the average OOHCA patient (i.e. those with agonal respirations).

### P304

### Cardiopulmonary resuscitation training: the need for continued education and training

**A Turley, G Bone, L Garcia, M de Belder, J Gedney**
*James Cook University Hospital, Middlesbrough, UK*
*Critical Care* 2005, **9(Suppl 1):**P304 (DOI 10.1186/cc3367)

**Introduction** Cardiopulmonary resuscitation (CPR) has a poor survival rate that may in part be due to flawed technique and training [1]. Recent recommendations for education and training have been issued for staff with responsibility for resuscitating patients [2]. These include 'staff with patient contact should be given regular resuscitation training appropriate to their expected abilities and roles', and 'cardiopulmonary arrest should be managed according to national guidelines'. The use of human patient simulators has become increasingly common in medical education [3]. Their use for exposing staff to high-risk complex clinical situations such as CPR is advocated by the department of health [4].
**Aims and methods** The aim of this study was to assess the resuscitation skills of all trainee junior doctors rotating through a 20-bed adult critical care unit (ITU/HDU) against current UK advanced life support (ALS) guidelines. Over an 18-month period, trainees underwent a compulsory CPR competency assessment by simulation testing, observed by two experienced ALS instructors following a refresher seminar. The trainees were assessed on basic life support (BLS), defibrillator safety and ALS skills in a scenario-

based format. Only candidates who passed each section were assessed on the next. All trainees were active members of the hospital cardiac arrest teams.

**Results** During the study period 32 trainees were assessed, of which 25/32 (78%) held a valid ALS certificate. BLS testing was inadequate in 2/32 (6%). Safety of defibrillation was failed by 7/30 (23%) of trainees. A full CPR scenario was given to 23 trainees. Of these 7/23 (30%) failed the scenario. Of the group as a whole 16/32 (50%) required further training and re-testing. Of those candidates who held a valid ALS certificate 10/25 (40%) failed the competency based assessment and required further training and re-testing.

**Conclusions** Junior medical staff require regular scenario-based CPR training. This study demonstrates that skills acquired during life support training are not retained and regular competency-based assessment is required irrespective of previous resuscitation training. Repeated scenario-based competency assessments should be a compulsory requirement of all trainee posts.

**References**

1. *Resuscitation* 1998, **37:**173-175.
2. *Standards for Clinical Practice and Training*. Resuscitation Council (UK); 2004.
3. *Hospital Med* 2003, **64:**677-681.
4. *Building a Safer NHS for Patients*. London: Department of Health; 2001.

## P305

### Effectiveness of an intubating laryngeal mask airway (ILMA Fastrach) used by nurses during out-of-hospital cardiac arrest resuscitation

**M Vergnion, S Thoumsin, V Fraipont**
*CHR Citadelle, Liège, Belgium*
*Critical Care* 2005, **9(Suppl 1):**P305 (DOI 10.1186/cc3368)

**Introduction** ILMA Fastrach is a good alternative to difficult endotracheal intubation even by an untrained physician but has never been studied in a out-of-hospital setting. Our aim was to evaluate the efficiency of this device used by untrained nurses in out-of-hospital cardiac arrest (OHCA).

**Method** After a brief instruction course and training on a mannequin, 12 nurses used ILMA Fastrach during 71 OHCA(s) resuscitation in a prospective open study. Procedure took place under the supervision of a certified emergency physician while ambulance officers applied basic life support. The ILMA size was selected according to the manufacturer's instructions and they were lubricated before insertion. Effective ventilation after mask insertion was verified by presence of ample chest movement and correct intubation was verified by the physician (chest auscultation) and by capnography. A digital voice recorder recorded speed and success rates. After two unsuccessful attempts, the physician performed classic intubation.

**Results** Effective ventilation after mask insertion was obtained in 97% (65/67); in the two unsuccessful cases, one was hanged and one had a literalised larynx (these data were not collected in four patients because of a recording problem). The rate of successful endotracheal intubation was 75% (53/71) after the first attempt and 89% (63/71) after the second. In the eight unsuccessful cases, ventilation with the mask was effective. The total mean time of intubation (since inclusion) was 148 s with a mean time of 53 s to prepare the device. The physician easily intubated all the eight remaining patients: a cephalic larynx was noticed in the five cases (mask size 5 chosen), one was hanged, and no abnormalities were in the two others.

**Conclusion** The ILMA Fastrach is a good alternative to classical intubation by untrained nurse OHCA resuscitations. The patient could be ventilated after mask insertion in most cases and the time to perform intubation is short. However, 1 min is necessary to prepare the device, so a good training and preparation of the material is necessary. Results are not as favourable as in the operative room and the effectiveness of ventilation with the mask was not predictive of intubation. However, only two unsuccessful attempts were permitted before classical intubation and the size according to the weight was inadequate in five cases. A large multicenter study is warranted to confirm these results.

## P306

### Use of automated external defibrillators in the House of Representatives Brazil, the first in Latin America: a 2-year experience

**S Timerman[1], A Quilici[1], M Gonzalez[1], L Hargreaves[2], J Ramires[1]**
*[1]Heart Institute (InCor), Sao Paulo, Brazil; [2]House of Representatives Medical Department, Brasilia – DF, Brazil*
*Critical Care* 2005, **9(Suppl 1):**P306 (DOI 10.1186/cc3369)

**Background** Passengers who have ventricular fibrillation aboard commercial aircraft rarely survive, owing to the delay in obtaining emergency care and defibrillation.

**Methods** In 2002, after the incorporation of automated external defibrillators (AEDs) by other PAD initiatives, a major Latin American House of Representatives (HR) began equipping its major building (Chamber of Deputies) – 513 Representatives, around 5000 people working and more than 20,000 people transiting every day – with automated external defibrillators (Lp 500). We chose the healthcare professional (more than 30) as the focus of the training program conducted according to the guidelines of the American Heart Association in the use of the defibrillator and applied the device when people had a lack of consciousness, pulse, or respiration. The AEDs were also used as a monitor for other medical emergencies, generally at the direction of a physician. We placed a separate cardiac monitor without the capacity for defibrillation, to be used when the strict definition of cardiac arrest has not been met (Lp 12). The electrocardiogram that was obtained during each use of the device was analyzed by two physicians for appropriateness of use. We analyzed data on all six instances in which the defibrillators were used between 1 February 2002 and 1 September 2004.

**Results** Automated external defibrillators were used for six patients, including six patients in ventricular fibrillation with documented loss of consciousness. Electrocardiographic data were available for all patients. The administration of shock was advised in all six patients who had electrocardiographically documented ventricular fibrillation (sensitivity and specificity of the defibrillator in identifying ventricular fibrillation, 100%). One patient had atrial flutter with high-degree atrioventricular block. All six episodes of ventricular fibrillation were properly treated with establishment of a final rhythm potentially perfusional in five cases. The first shock successfully defibrillated the heart in six patients (100%). No complications arose from use of the automated external defibrillator as a monitor in conscious passengers.

Of the six patients, four (66%) left the locality alive and three (50%) were discharged home from hospital. In all cases the initial rhythm was ventricular fibrillation.

**Conclusions** The use of the automated external defibrillator in the HR is effective.

## P307

### Synchronized cardioversion in a prehospital setting: a safe and reliable method for urgent treatment of tachyarrhythmias

**A Jelatancev[1], S Grmec[1], P Klemen[1], M Kovac[2]**
*[1]Centre for Emergency Medicine, Maribor, Slovenia; [2]Prehospital Emergency Unit, Ljubljana, Slovenia*
*Critical Care* 2005, **9(Suppl 1):**P307 (DOI 10.1186/cc3370)

**Objective** Synchronized cardioversion (SCV) is a useful and reliable method of converting atrial or ventricular tachycardia to sinus rhythm. It is a method of choice in patients who are at high risk of the arrhythmia and therefore require urgent treatment. Conscious patients must be well sedated.
**Design and setting** A prospective clinical investigation.
**Patients and methods** All adult patients (>18 years) were treated by an emergency physician in the prehospital setting. Indications for SCV were: arrhythmia with severe chest pain and/or shortness of breath, congestive heart failure, pulmonary congestion, decreased level of consciousness (reduced cerebral blood flow), systolic blood pressure less than 90 mmHg, shock, or acute myocardial infarction (AMI). Conscious patients were sedated or anaesthetized with midazolam and morphine, etomidate or propofol.
**Results** Over a period of 2 years, 22 patients have required SCV. Indications for SCV included 10 (45.5%) patients with atrial fibrillation (AF) with high risk, seven (31.8%) patients with supraventricular tachycardia (SVT) and five (22.7%) patients with ventricular tachycardia (VT) with pulse. Heart rates in AF and VT were more than 150 beats/min and in SVT more than 200 beats/min. In all patients two or more adverse signs of tachy-arrhythmia have been observed: congestive heart failure and/or pulmonary congestion in eight (36.4%) patients, hypotension and/or shock in 15 (68.2%) patients, severe chest pain or AMI in 10 (45.5%) patients; decreased level of consciousness in nine (40.9%) patients. The SCV was successful in all cases (in 19 cases in the first shock with 100 J, in two cases in the second shock with 200 J and in one case in the third shock with 360 J). All patients were hospitalized and left the hospital without any complications.
**Conclusion** SCV is a useful and safe method in treatment of unstable tachyarrhythmia in a prehospital setting. This is very important information, because in such situations the universal recommendation of the ILCOR 2000 International Guidelines for immediate cardioversion is the method of choice rather than a trial of antiarrhythmics.

## P308

### Prehospital transcutaneous cardiac pacing in bradycardia and asystole

**C Febra, A Lufinha**
*Hospital S Francisco Xavier SA, Lisbon, Portugal*
*Critical Care* 2005, **9(Suppl 1):**P308 (DOI 10.1186/cc3371)

**Background** Transcutaneous external cardiac pacing (TECP) provides a noninvasive, safe and rapid ventricular pacing, although there is controversy on the results observed both in hemodynamically significant bradycardia and asystole situations. The purpose of this study is to examine the success of TECP in our prehospital emergency medical team (VMER) practice, at Hospital S Francisco Xavier.
**Methods and results** In this retrospective cohort study, we examined 46 patients submitted to TECP between January 2001 and November 2004 with a median age of 68.6 years (40–94 years). The mean call-to-arrival time was 7.8 min, and cardiac arrest was present at our arrival in 43.5% of the cases and bradycardia with hemodynamic repercussion in 56.5%, manifested, p.e., as syncope (61.5%), chest pain (23%) and/or dyspnoea (15.4%). In the cardiac arrest situations, classic advanced cardiac life support was always provided, resulting in electromechanical disassociation (40%), asystole (15%) and complete AV blocking (15%), present immediately before pacing. There was a survival rate in the field of 40% of these patients, of whom 75% were hemodynamically stable at hospital admission. In the bradycardia cases, complete AV blocking was the most common presenting rhythm (73%), the mean heart rate was 33 ppm, and 76.9% of patients had shock criteria. Atropine was used unsuccessfully in 61.5% of patients. The TECP resulted in hemodynamic stability in 53.8%, death in the field in 15.4% and sustained shock in 30.8%. The overall success rate of TECP in these two groups, defined as hospital admission, was 65.2%.
**Conclusions** In cardiac arrest events, TECP was associated with a better survival rate on the field than our global survival rate on the field (21%). This may be due to its utilisation mainly in electromechanical disassociation and younger patients. TECP results in a correct cardiac output in much of severe bradycardia situations, allowing a stable transportation to the hospital where it may be kept or changed by other pacing approaches.

## P309

### EMERGE™: a multiprofessional training course in the care of the acute coronary syndrome patient

**S Timerman[1], M Moretti[1], F Marques[1], R Ramos[2], E Mesquita[3], E Stefanini[4], C Gun[2], F Tarasoutchi[1], E Paiva[5], D Ferreira[5], A Timerman[2]**
*[1]Heart Institute, Sao Paulo, Brazil; [2]Dante Pazzanese Institute of Cardiology, Sao Paulo, Brazil; [3]Hospital Pró Cardiaco, Rio de Janeiro, Brazil; [4]UNIFESP, Sao Paulo, Brazil; [5]NRC, Sao Paulo, Brazil*
*Critical Care* 2005, **9(Suppl 1):**P309 (DOI 10.1186/cc3372)

The Acute Coronary Syndrome (ACS) Recognition and Treatment (EMERGE™) course is a 1-day (3 hours) course originally designed to give doctors greater confidence and ability in the recognition and management of adult patients who have ACS. It may also be suitable for many other groups of health professionals. EMERGE™ was developed using principles common to many advanced life support courses and incorporates aspects of clinical governance, multidisciplinary education and interprofessional working. It incorporates precourse reading, informal and interactive seminars, and role-play during three clinically based scenarios. A novel aspect of EMERGE™ is that participants undertake role interchange during scenarios, thereby facilitating mutual understanding. At all times during the course, participants are encouraged to reflect on their actions and to pay particular attention to detail.
Using initial and final theoretical written test, after the 3-month courses (36 courses), we assessed the knowledge of aspects of ACS among 900 doctors. The average (± standard deviation) knowledge score was higher for those who had completed an EMERGE™ course, pre-test (545 students) = 23.8 (8.44 ± 1.30) points and post-test (834 alunos) = 25.3 (9.85 ± 2.12) points ($P < 0.05$). In addition, those in the post-EMERGE™ group also showed significantly better knowledge about ACS (85.6% [714 doctors]) acquired skills in treatment an ACS. We have demonstrated evidence that doctors' knowledge of ACS can be improved by attending courses such as EMERGE™.

## P310

### High mortality rate in critically ill medical patients with new-onset atrial tachyarrhythmias despite rapid conversion to sinus rhythm

**M Sleeswijk, J Tulleken, T v/d Werf, J Ligtenberg, T v Noord, J Zijlstra**
*AZG, Groningen, The Netherlands*
*Critical Care* 2005, **9(Suppl 1):**P310 (DOI 10.1186/cc3373)

**Introduction** New-onset atrial tachyarrhytmia (AT) is frequently seen in critically ill surgical patients (incidence 10.2%) and associated with high mortality rate (23.4%). Whether this also applies to medical ICU patients is unclear. In a follow-up study all medical patients with AT were evaluated.
**Methods** In a 12-bed medical ICU, all consecutive patients with AT were evaluated during a 4-month period. Characteristics, response to treatment and outcome were registered. All patients with AT were treated with $MgSO_4$-amiodarone after correction of predisposing factors; $MgSO_4$ bolus (0.037 g/kg) followed by continuous infusion (0.025 g/kg). Those with persistent AT >110 beats/min after 1 hour were given intravenous amiodarone (bolus 300 mg) followed by continuous infusion (1200 mg/24 hours).
**Results** One hundred and forty-seven patients were admitted for medical reasons. AT was seen in 14 patients. The most common reason for ICU admission was sepsis (nine patients). Patient characteristics are presented in Table 1. Two patients converted after fluid repletion. Ten patients received the treatment protocol. Five patients converted after magnesium therapy, and addition of amiodarone was given to five patients. All patients converted within 24 hours (median [range] 2.5 [1–19]). Ten patients died during their hospitalization. Time between the onset of AT and death was 7.7 ± 5.5 days (mean ± standard deviation [SD]).

**Table 1**

| | |
|---|---|
| Male/female | 6/8 |
| Age (mean ± SD) | 64 ± 20 years |
| APACHE II (mean ± SD) | 24 ± 8 |
| Rhythm (AF/flutter/SVT) | 11/1/2 |
| Norepinephrine | 11 |
| MAP before/after AT (mean ± SD) | 82 ± 13/65 ± 13 mmHg |
| Heart rate before/after AT | 99 ± 19/148 ± 37 beats/min |
| Serum $K^+$ (mean ± SD) | 4.10 ± 0.5 mmol/l |
| Serum $Mg^{2+}$ (mean ± SD) | 0.85 ± 0.12 mmo/l |

**Conclusion** The incidence of AT in this patient cohort was 14/147. Mg-amiodarone is a highly effective regimen for conversion. Despite this, mortality was high and therefore AT was not the cause of death but rather an epiphenomenon. Compared with surgical patients, medical patients had a much higher mortality rate.

## P311

### Troponin incidence, prevalence and prognosis among critically ill patients

**W Lim, L Griffith, M Crowther, P Devereaux, D Cook**
*McMaster University, Hamilton, Canada*
*Critical Care* 2005, **9(Suppl 1):**P311 (DOI 10.1186/cc3374)

**Background** The diagnosis of acute myocardial infarction (AMI) in critically ill patients is usually dependent on the presence of ischemic changes on an electrocardiogram (ECG) and measurement of biochemical markers such as troponin. Among patients in the ICU, there is uncertainty surrounding the significance of elevated troponin values, their relation to coronary ischemia and infarction, and the prognostic and therapeutic implications.
**Objective** To document the prevalence and incidence of elevated troponin levels in critically ill patients correlated with ECG findings (presence of ischemic changes [AMI], non-ischemic ECG changes, and normal ECG), and to evaluate the morbidity and mortality outcomes of each of these categories compared with patients with normal troponin values.
**Methods** We conducted a retrospective chart review of 198 patients from 261 critically ill patients admitted to a university-affiliated, general medical–surgical ICU who were enrolled in a prospective cohort study evaluating the prevalence and incidence of deep vein thrombosis.
**Data extraction** We reviewed daily medical records during the patient's ICU admission for signs and symptoms of AMI, laboratory and radiologic investigations, and collected morbidity and mortality outcomes.
**Results** The prevalence of all elevated troponin levels was 36.4%; 19.2% had AMI (elevated troponin with ischemic ECG changes), 14.7% had elevated troponin without typical ischemic ECG changes, and 1.5% had elevated troponin and a normal ECG. The incidence of AMI over the ICU stay was 6.2%, of which 42% were diagnosed with AMI on admission (i.e. they had recurrent AMI). Morbidity (length of stay [LOS]) and mortality outcomes in patients with elevated troponin and associated ECG findings compared with patients with normal troponin are presented in Table 1.

**Table 1**

| Outcomes | Ischemic ECG ($n = 45$) | Non-ischemic ECG ($n = 30$) | Normal ECG ($n = 3$) | Normal troponin ($n = 104$) |
|---|---|---|---|---|
| ICU LOS, median (IQR) | 10 (8, 18) | 8 (4, 14) | 4 (3, 39) | 10 (6, 18) |
| Hospital LOS, median (IQR) | 20 (11, 54) | 13.5 (10, 31) | 40 (12, 114) | 30 (15, 61) |
| ICU mortality, *n* (%) | 15 (33.3) | 11 (36.7) | 1 (33.3) | 21 (20.2) |
| Hospital mortality, *n* (%) | 20 (44.4) | 13 (43.3) | 1 (33.3) | 35 (33.7) |

**Conclusions** Elevated troponin levels are common in the critically ill, yet it is unclear under what circumstances they represent an adverse prognostic marker for ICU and hospital mortality. Additional studies are needed to determine the significance of elevated troponin values in the presence and absence of ECG changes, evaluating long-term outcomes and the efficacy of anti-ischemic treatments in critically ill patients.

## P312

### Clinical determinants of severe bleeding complications in patients with acute myocardial infarction treated with thrombolytic therapy

**J Rossinen[1], J Viita[2], M Nieminen[1], R Lassila[1]**
*[1]Helsinki University Hospital, Helskinki, Finland; [2]Medical Faculty, Turku, Finland*
*Critical Care* 2005, **9(Suppl 1):**P312 (DOI 10.1186/cc3375)

The aim of the study was to determine the frequency of bleeding complications in a clinical setting, and to clarify the practise in laboratory monitoring of haemostasis (TT%, APTT, HCR) in patients with acute myocardial infarction who are treated with fibrinolytics. In this clinical, retrospective series we included randomly 301 patients who were treated during the years 2000–2003 due to acute myocardial infarction in the Helsinki University Central Hospital. Two hundred and forty (80%) of the patients were treated with a thrombolytic therapy. Six (3%) patients received thrombolytic therapy

despite them having an absolute contraindication, and 75 (31%) received it while having a relative contraindication. The incidence of cerebral bleeding during the first 48 hours was unexpectedly high (2.5%). The incidences of bleeding complications are presented in Table 1. The parameters of haemostasis could not predict bleeding complications in our study, probably due to low rate of measurements prior to fibrinolytic therapy. It is therefore important to strictly follow the guidelines of thrombolytic therapy in patients with acute ST-elevation myocardial infarction. Routines for laboratory monitoring of haemostatic variables are to be implemented to improve safety and early detection of bleeding complications.

**Table 1**

| | Thrombolysis group | Non-thrombolysis group |
|---|---|---|
| Intracerebral bleed | 6 (2.5%) | 1 (1.6%) |
| GI haemorrhage | 21 (8.8%) | 3 (4.9%) |
| Unexplained bleed | 24 (11%) | 14 (23%) |

## P313

### Facilitated percutaneous coronary intervention: a new treatment strategy for acute myocardial infarction

**H Khaled Nagi, M Shehata, A ElSherif, M Ashraf, M ElBadry, S Mokhtar**
*Cairo University, Cairo, Egypt*
*Critical Care* 2005, **9(Suppl 1):**P313 (DOI 10.1186/cc3376)

Restoring patency of infarct-related artery (IRA) is the ultimate goal of all cardiologists. Such a goal can be achieved either pharmacologically 'using thrombolytic therapy' or through percutaneous coronary intervention (PCI). The latter needs a sophisticated setup, an equipped cath lab and a skilled team. Such a system might not be always available, and a full-dose thrombolytic therapy is the next best alternative. There has recently been a trend towards 'facilitated PCI' whereby low-dose thrombolytic and/or antiplatelet therapies are used prior to primary PCI, aiming at an early, complete, and sustained epicardial flow and myocardial perfusion.

To compare the efficacy and safety of facilitated PCI with standard primary PCI, we studied 40 patients with acute myocardial infarction (AMI) divided into two groups, a study group consisting of 20 patients (18 males, two females, mean age 46.3 ± 11.5 years), all received 750,000 u streptokinase combined with GP IIb/IIIa receptor inhibitor 'tirofiban' 0.4 μg/kg/min over 30 min followed by 0.1 μg/kg/min over 48 hours. Twenty patients (15 males, five females, mean age 54 ± 8.6 years) served as control group (no thrombolytic nor antipaltelet therapy). Both groups underwent PCI within (73 ± 18 min) from randomization. Angiographic patency was expressed in terms of TIMI flow grading system, ECG criteria comprised extent and rapidity of ST-segment resolution, and laboratory criteria involved early peaking of CK-MB within 12 hours from randomization. Besides clinical evaluation in terms of major adverse cardiac events, echocardiographic parameters (LVEDD and LVEF) were used to assess LV function before and after PCI and monthly thereafter for 6 months.

Compared with the group subjected to PCI alone, those who had preceding adjunctive pharmacological therapy 'facilitated PCI' exhibited significantly greater TIMI 3 flow (84% vs 60%, $P < 0.05$), smaller LVEDD (5.0 vs 5.5, $P < 0.05$), significantly higher LVEF (55.4% vs 50.7%, $P < 0.05$) and lower rate of MACE (0% vs 20%). Patients with facilitated PCI also exhibited significantly higher ST-segment resolution (58% vs 45%, $P < 0.05$) and earlier peaking of CK-MB (85% vs 35%) compared with control group.

In conclusion, facilitated PCI offers an excellent way of circumventing the time delay preceding PCI that is frequently encountered on hospital admission of patients with acute MI. Through combining interventional, fibrinolytic and GP IIb/IIIa inhibitor therapy, facilitated PCI provides more rapid, complete and sustained patency of IRA than primary PCI alone without the adverse effects of full-dose thrombolytic therapy and with a better outcome in terms of lesser MACE and preserved LV function.

## P314

### Left ventricular remodeling and function after primary and delayed PCI in patients with recent myocardial infarction

**M Hamila, M Badry, S Fawzy, H Nagi, T Gohary, K Hussein**
*Faculty of Medicine, Kasr El Aini Hospital, El Manial Cairo, Egypt*
*Critical Care* 2005, **9(Suppl 1):**P314 (DOI 10.1186/cc3377)

**Background** It has been well established that restoration of patency of an infract-related artery by percutaneous intervention as early as possible in patients with recent myocardial infarction may preserve left ventricular global function and also prevent LVEDV progressive increase and remodeling,

**Aim** To evaluate and compare the effect of primary and delayed PCI in patients with recent myocardial infarction (MI).

**Methods** Forty patients were included in the study with first anterior MI; they were divided into group A who had the chance of undergoing primary PCI within less than 12 hours of start of chest pain with mean 5.4 hours and a door to balloon time of 1.6 hours, and group B who due to out of hand circumstances neither received thrombolytic therapy nor arrived at hospital within 12 hours, but were scheduled as routine PCI with mean 20.7 days. The left ventricular function and dimensions were assessed by serial echocardiographic readings measuring LVEDV, LVESV, EF and RWMI at 24 hours of admission and after 3 months and 6 months. Results were expressed as mean ± standard deviation and $P < 0.005$ was considered significant.

**Results** First echo results at baseline showed no significant difference of LVEDV, RWMI and EF in both group A and group B, that indifference was also remarkerable at echo done at 3 months with $P = 0.6$, while at 6 months reading the LVEDV in group A showed a significant decrease (115 ± 32.14 vs 138 ± 32.96, $P = 0.048$). Ejection fraction difference between two groups were not significant at baseline echo, but improved significantly at 3 and 6 months (58.5 ± 4.5 vs 55.2 ± 6.4, $P = 0.046$ at 3 months and 59.5 ± 6.81 vs 51.88 ± 10.7, $P = 0.008$ at 6 months, respectively). RWMI results started to improve significantly from 3 months to 6 months in group A versus group B (1.27 ± 0.13 vs 1.38 ± 0.18, $P = 0.032$ at 3 months) but at 6 months there was no further improvement with $P = 0.6$

**Conclusion** Although the recent evolvement and the theory of opening of IRA whatever the timing, primary PCI has superiority in preventing LV remodeling and preserving global LV function

## P315

### Acute myocardial infarction: incidence and outcomes in an intensive care unit

**I Qushmaq[1], W Lim[1], P Devereaux[1], M Crowther[1], A Tkaczyk[2], K Lutz[1], E McDonald[2], J Hancock[1], D Heels-Andsell[1], D Cook[1], for the Troponin T Trials Group**
*[1]McMaster University, Hamilton, Canada; [2]St Joseph's Hospital, Hamilton, Canada*
*Critical Care* 2005, **9(Suppl 1):**P315 (DOI 10.1186/cc3378)

**Objective** To enhance the precision of the definition of acute myocardial infarction (AMI), the European Society of Cardiology/American College of Cardiology (ESC/ACC) recently updated the

diagnostic criteria for AMI. Given this change in AMI diagnostic criteria, little is known about the current incidence of AMI in the ICU and the associated clinical outcomes. We undertook a study to inform these issues.
**Design** A prospective 2-month cohort study.
**Setting** A 15-bed closed university-affiliated medical–surgical ICU.
**Methods** We enrolled all consecutive ICU patients from 12 July to 12 September 2004. All aspects of patient management were at the discretion of the ICU team, which was unaware of the study to limit any influence on ECG or troponin test-ordering practices. As clinically indicated, 12-lead ECGs were performed by a technologist during the day, or by the ICU bedside nurse for emergencies, during the evenings and weekends. We adapted the Joint ESC/ACC redefinition of AMI for the ICU setting. Two investigators independently classified all patients as AMI or no AMI; discordance was resolved by discussion and criterion review. We used Wilcoxon Two-Sample Rank Sum Test to test for differences in continuous variables and Fisher's Exact Test for dichotomous variables.
**Result** We screened 117 ICU admissions but considered only the first admission of two patients who were admitted twice. We enrolled 115 patients aged 64.1 (± 17.2) years with an APACHE II score of 21.9 (± 9.8); 83 (72.2%) patients were medical. Overall ICU mortality was 21.7% and hospital mortality was 27.8%. Of 115 patients 93 (80.9%) patients had both at least one ECG performed and one troponin measurement during ICU admission, seven (6.1%) patients had at least one ECG performed but no troponin measurement, 11 (9.6%) patients had at least one troponin measurement but no ECG performed, and four (3.5%) patients had neither an ECG nor troponin. Using the ESC/ACC criteria adapted to the ICU setting, 24 of 115 (20.9%) patients developed AMI (crude agreement between adjudicators was 88%).

**Table 1**

| Outcome | AMI ($n = 24$) | No AMI ($n = 91$) | $P$ value |
|---|---|---|---|
| Duration of MV | 2 (1–6) | 2 (0–5) | 0.32 |
| Duration of ICU | 4.5 (2–8) | 4 (2–6) | 0.62 |
| ICU mortality | 9 (37.5%) | 16 (17.6%) | 0.05 |
| Hospital stay | 18 (4.5–4.1) | 12 (7–21) | 0.34 |
| Hospital mortality | 12 (50%) | 20 (22.0%) | 0.01 |

**Conclusion** One-fifth of these medical–surgical critically ill patients sustained an AMI. Patients with AMI had a significantly higher mortality than those who did not. More research is needed on appropriate AMI definitions in the ICU setting, risk factors, detection methods, mechanisms of myocardial necrosis during critical illness, optimal prevention and treatment strategies, and long-term prognosis.

### P316

### Clinical features of acute myocardial infarction in patients with cor pulmonale

**Y Zhao, L Lu, L Liou, Q Xue**
*Institute of Geriatric Cardiology, Chinese PLA General Hospital, Beijing, China*
*Critical Care* 2005, **9(Suppl 1):**P316 (DOI 10.1186/cc3379)

**Objective** To investigate the clinical features of acute myocardial infarction (AMI) in patients with cor pulmonale.
**Methods** Manifestations of AMI in 30 patients with cor pulmonale (observation group) was compared with that of 171 patients with AMI only (control group).
**Results** There were more smokers in the observation group than in the control group (60.0% vs 35.1%, $P < 0.05$). The incidence of chest pain in observation group was significantly lower than that in the control group (16.7% vs 43.9%, $P < 0.001$), but the incidence of dyspnoea was significantly higher than that in the control group (50.0% vs 16.4%, $P < 0.001$). The serum albumin and ferrohemoglobin were lower in the observation group than those in the control group (33.2 ± 9.1 vs 37.8 ± 6.0 g/l, $P < 0.01$ and 127.2 ± 18.9 vs 134.9 ± 17.7 g/l, $P < 0.05$, respectively). Acute pulmonary edema was more common in the observation group than those in the control group (46.7% vs 22.2%, $P < 0.01$). Of 30 patients in the observation group 33.3% were accompanied with serious lung infection but only 8.8% in the control group. The mortality in the observation group was higher than that in the control group (23.3% vs 13.5%, $P = 0.161$), but there was no statistically significant difference between the two groups.
**Conclusions** Infection, anemia and hypoproteinemia are important precipitating factors in acute myocardial infarction characteristic of painlessness in patients with cor pulmonale. Acute left ventricular failure can be the initial symptoms of AMI in patients with cor pulmonale. Because of its high mortality and poor prognosis, more attention should be paid to these symptoms.

### P317

### Prospective study on myocardial infarction: short-term prognostic factors

**M Zare[1], N Kianmehr[1], A Hosseinnejad[1], D Farsi[1], A Arhamidolatabadi[2], F Bozorgi[2]**
*[1]Iran University of Medical Sciences, Tehran, Iran;*
*[2]Beheshti University of Medical Sciences, Tehran, Iran*
*Critical Care* 2005, **9(Suppl 1):**P317 (DOI 10.1186/cc3380)

**Introduction** MI is one of the major causes of mortality and morbidity worldwide. Our resources in approaching and treating this entity are restricted due to financial causes. Studying the risk factors helps to improve health services and to provide better care where most needed.
**Methods and materials** In this observational longitudinal study patients with diagnosis of acute MI admitted at Rasoul akram ED during 21 months were included. The risk factors, primary and secondary endpoint outcomes were registered on a form. Primary endpoints were defined as death and need to CPR, and secondary endpoints were defined as death, asymptomatic, CCU admission, need to CPR, and angiography result when it was performed. Two months later, secondary endpoints were followed-up by telephone.
**Results** One hundred and fifty-four patients were included. Twenty-one percent of patients died. Low Hgb level ($P = 0.037$) and leukocytosis ($P = 0.011$) are related to patient death. Mean age was 70.5 ± 2.28 and 56.5 ± 1.06 years in dead and alive patients, respectively ($P = 0.000$). Angiostenosis, previous MI and heart failure increase the mortality risk to 10 times ($P = 0.000$), 3.8 times ($P = 0.01$) and 3.2 times ($P = 0.003$), respectively. Mean interval time between appearance of the symptoms and fibrinolytic therapy in ST-elevation MIs was 2.31 (± 0.22) hours, there was no mortality when fibrinolytic therapy was started less than 0.5 hours from symptoms, and only one mortality when it was started at less than 1 hour. Sex distribution was not related to either primary or secondary endpoint outcomes. There was no relationship between patients' 2-month survival and HTN, DM, HLP, dysrhythmia, blocks, ST elevation, involved aspect of the heart and fibrinolytic therapy.
**Discussion** Mean age > 70 years, angiostenosis, previous MI, heart failure, low Hgb level and leukocytosis are associated with poor prognosis in MI patients. Early thrombolytic therapy decreased mortality but has no effect on 2-month outcome.

## P318

### Haemoglobin concentration on admission influences the rate of inhospital 30-day mortality and complications in patients with acute myocardial infarction: a retrospective analysis of 637 Chinese patients

**Y Zhao, J Ma, S Wang, Q Xue, W Gao, Y Li**
*Institute of Geriatric Cardiology, Chinese PLA General Hospital, Beijing, China*
*Critical Care* 2005, **9(Suppl 1):**P318 (DOI 10.1186/cc3381)

**Objective** To determine the association between haemoglobin concentrations on admission and inhospital 30-day cardiac mortality and complications among patients with acute myocardial infarction during their hospital course.
**Methods** We conducted a retrospective study of data on 637 Chinese patients who were hospitalized with acute myocardial infarction. Patients were categorized according to the haemoglobin concentration on admission (<12 g/dl, mean ± standard deviation 10.5 ± 1.4 g/dl; 12–13.9 g/dl, mean ± standard deviation 13 ± 0.6 g/dl; 14 g/dl or greater, mean ± standard deviation 15.2 ± 0.9 g/dl), and data were evaluated to determine whether there was an association between the haemoglobin concentrations on admission and inhospital 30-day mortality and complications. Complications were defined as cardiogenic shock, congestive heart failure, arrhythmia, ventricular tachycardial or fibrillation and pneumonia.
**Results** Patients with lower haemoglobin concentrations on admission had higher inhospital 30-day mortality rates ($P < 0.001$). Inhospital 30-day mortality was 21.4% in patients with haemoglobin concentrations <12 g/dl, 11.6% in patients with haemoglobin concentrations of 12–13.9 g/dl, and 5.3% in patients with haemoglobin concentrations 14 g/dl or greater. The increase in risk of complications associated with a low haemoglobin concentration was more pronounced in patients with anaemia than in patients without. Compared with patients with haemoglobin concentrations 14 g/dl or greater, those with haemoglobin concentrations <12 g/dl and 12–13.9 g/dl had more inhospital complications, including arrhythmia, congestive heart failure and pneumonia (40.5% versus 33.8% versus 23.1%, $P = 0.001$; 28.2% versus 20.0% versus 8.2%, $P < 0.001$; and 26.7% versus 8.4% versus 2.8%, $P < 0.001$, respectively). As expected, a significant inverse correlation between haemoglobin concentrations and ages was observed in the patients with acute myocardial infarction ($r = -0.51$; $P < 0.001$).
**Conclusions** The traditional belief is that anaemic patients with coronary artery disease are at high risk for myocardial ischaemia or infarction because they cannot increase oxygen extraction or augment coronary arterial flow. It is demonstrated in this study that a low haemoglobin concentration on admission increases the risk of death or serious complications in the patients with acute myocardial infarction. There is a greater incidence of patients with a low haemoglobin concentration on admission in the elderly patient than that in the younger one.

## P319

### Protective effects of hemodilution and ischemic preconditioning against reperfusion injury in pig heart

**W Xiangrui**
*Renji Hospital, Shanghai, China*
*Critical Care* 2005, **9(Suppl 1):**P319 (DOI 10.1186/cc3382)

**Objective** We investigated the protective effects of isovolumetric hemodilution and ischemia preconditioning against myocardial injury due to reperfusion through a pig myocardial ischemia reperfusion model.
**Methods** Eighteen mini-pigs were used in an acute myocardial ischemia model. They were randomly divided into three groups, with six pigs in each group: the control (group I, $n = 6$), ischemia pre-treatment (group II, $n = 6$), ischemia pretreatment plus blood dilution (group III, $n = 6$). Cardiac output (CO), saturation of mixed venous blood oxygen ($SvO_2$) and blood flow of coronary artery were measured, and then the oxygen supply to the myocardium and the oxygen consumption were calculated. The amount of malondialdehyde (MDA), the superoxide dismutase (SOD) activity, the creatine phosphokinase (CPK) and creatine phosphokinase isoenzyme (CK-MB) were also determined 20 min and 60 min, respectively, before and after the forceps clamping. A sample was taken from the left atrial appendage to determine the rate of expression of heat shock proteins Hsp70 mRNA.
**Results** When ischemia lasted for 20 min, the heart rate (HR) of group I and group II slowed down dramatically while that of group III accelerated slightly. The MAP, CI and SVR of all three groups significantly decreased from control values ($P < 0.01$), but the magnitude of decrease in groups II and III were lower than those of group I ($P < 0.05$). Also the SVR of group III was significantly lower than group II ($P < 0.05$). After reperfusion at 20 min and 60 min, the HR of groups I and II was significantly lower than that of the controls ($P < 0.01$). The HR of group III was significantly higher than that of groups I and II ($P < 0.05$), but was not significantly higher than the control value ($P > 0.05$). The decreased MAP and CI of groups II and III were significantly lower than those of group I ($P < 0.05$). In addition the SVR of group III was lower than groups I or II ($P < 0.05$). The values of CPK, CPK-MB of all three groups were significantly higher than the controls after reperfusion at 20 min and 60 min ($P < 0.05$–$0.01$, respectively). However, groups II and III increased less than those of group I. The values of CPK and CPK-MB in group III were lower than that of group II ($P < 0.05$). The MDA value of group I was dramatically higher than that of groups II and III after reperfusion at 20 min and 60 min ($P < 0.05$), while the value of group III was lower than that of group II after reperfusion at 60 min ($P < 0.05$).The expression of Hsp70 mRNA in group II and group III was higher than that of group I ($P < 0.05$), and Hsp70 mRNA in group III was higher than group II ($P < 0.05$) after reperfusion at 20 min and 60 min.
**Conclusion** Isovolumetric hemodilution can increase the protection of preconditioning against ischemic myocardial injury caused by reperfusion.

## P320

### The reliability of electrocardiogram interpretation in critically ill patients

**W Lim[1], I Qushmaq[1], A Tkacyzk[1], L Donahoe[1], D Heels-Ansdell[1], J Hancock[1], E McDonald[1], M Crowther[1], P Devereaux[1], R Cook[2], D Cook[1]**
*[1]McMaster University, Hamilton, Canada; [2]University of Waterloo, Canada*
*Critical Care* 2005, **9(Suppl 1):**P320 (DOI 10.1186/cc3383)

**Background** Critically ill patients are generally unable to report ischemic chest pain due to decreased consciousness, endotracheal intubation, and use of sedatives and narcotics. The diagnosis of cardiac ischemia is therefore usually based on elevated cardiac enzymes and typical ischemic changes on an electrocardiogram (ECG). Although key management decisions depend on ECG interpretation, the reproducibility of ECG interpretation is unclear in the ICU.

**Objective** To estimate the inter-rater and intra-rater reliability of ECG interpretation for the presence of myocardial ischemia in critically ill patients, with and without knowledge of troponin T values.
**Design** A prospective cohort study.
**Setting** A 15-bed medical–surgical university-affiliated ICU.
**Patients** Consecutive adults admitted to the ICU over a 2-month period.
**Methods** We collated all consecutive 12-lead ECGs performed on all patients during the study period. Using a structured, pre-tested form, and blinded to patient data and each other's ratings, two internists interpreted each ECG. Two weeks later, both raters re-interpreted the same ECGs, blinded to their previous interpretation and unblinded to the troponin T values. We report results using chance-independent agreement (phi), which generates less biased agreement measures than chance-corrected agreement (kappa). Discrepancies for the two primary outcomes (presence of pathologic Q waves and the overall assessment of the presence of myocardial ischemia) and 13 secondary outcomes (other ECG abnormalities, such as ST segment changes) were resolved by a third internist blinded to the two previous ratings but unblinded to troponin T values.
**Results** We found variable inter-rater reliability of ECG interpretation when raters were blinded to troponin T levels. We report all values with the associated 95% confidence interval (CI). For the two primary outcomes, agreement was substantial (phi 0.61 [95% CI 0.17, 0.85]) for the detection of pathologic Q waves and slight (phi 0.10 [–0.06, 0.25]) for the overall assessment of the presence of myocardial ischemia. For secondary specific ECG changes, agreement was highest (phi 0.79 [0.64, 0.89]) for detection of a new left bundle branch block (LBBB) and lowest (phi 0.30 [0.003, 0.54]) for ST segment depression. When unblinded to troponin T values, inter-rater reliability increased slightly for each primary and secondary outcome. Intra-rater reliability, assessed prior to and following knowledge of troponin T levels, was high for detection of pathologic Q waves (phi 0.44 [0.08, 0.69] and 0.78 [0.68, 0.85], respectively), and new LBBB (phi 1.0 and 0.95 [0.83, 0.98], respectively), but was lower for the overall assessment of the presence of ischemia (phi 0.21 [0.06, 0.36] and 0.47 [0.34, 0.58], respectively).
**Conclusions** We found that the inter-rater and intra-rater reliability of ECG interpretation for the overall detection of specific ECG changes in critically ill patients was good but variable. However, for the overall assessment of the presence of myocardial ischemia, reliability was poor. Knowledge of troponin T levels appears to improve the reliability of ECG interpretation. Further studies evaluating the difficult diagnosis of myocardial ischemia in the critically ill are required.

## P321

## Patient selection for the ventricular assist device

**D Hall, P Vykaranam**
*Harefield Hospital, Harefield, UK*
*Critical Care* 2005, **9(Suppl 1):**P321 (DOI 10.1186/cc3384)

**Introduction** In addition to their use as a bridge-to-transplant, a bridge-to-recovery and as destination therapy, ventricular assist devices (VADs) are increasingly being used on patients 'in extremis' as a salvage procedure, as a bridge to a long-term device. We performed a retrospective analysis of the clinical criteria for VAD insertion in patients who have received devices.
**Methods** Data were collected for all patients receiving a VAD in the last year, excluding those patients with a previous transplant or VAD. On each patient the following data were collected: age and degree of urgency of referral, diagnosis and duration of illness, pre-operative systems review within 24 hours of device insertion, device inserted, and outcome.
**Results** Fifteen patients were included. Three groups of five patients emerged based on the referral pattern and duration of illness. Group 1, emergency (less than 2 weeks illness) – ischaemic and postpartum cardiomyopathy, acute myocardial infarction, myocarditis. Group 2, acute (less than 4 weeks illness) – postpartum and dilated cardiomyopathy. Group 3, elective (assessed for transplantation) – dilated and ischaemic cardiomyopathy. See Table 1.

**Table 1**

| | Group 1 | Group 2 | Group 3 |
|---|---|---|---|
| Age (mean) | 47.2 | 29.6 | 43.6 |
| CI (mean) | 1.2 | 1.3 | 1.4 |
| LVEF (mean) | 19% | 16.6% | 23.4% |
| Inotropes | 5/5 | 4/5 | 4/5 |
| IABP | 1/5 | 0/5 | 1/5 |
| Ventilated | 2/5 | 0/5 | 0/5 |
| Acidosis | 5/5 | 0/5 | 0/5 |
| Renal dysfunction | 4/5 | 1/5 | 3/5 |
| Liver dysfunction | 4/5 | 3/5 | 5/5 |
| Device | Levitronix | Heartmate I<br>Jarvik 2000 | Jarvik 2000<br>Heartmate I<br>Thoratec |
| Survival | 1/5 | 4/5 | 5/5 |

**Conclusion** Once patients require inotropic support, early referral is preferred. Recent onset renal and liver dysfunction due to poor ventricular function will be improved with a VAD. The onset of a metabolic acidosis is a predictor of poor outcome but a salvage procedure is possible in most patients with acute ventricular dysfunction.

## P322

## Prognostic factors of percutaneous cardiopulmonary support therapy at Osaka City General Hospital, Japan

**T Yoshida, M Satani, H Rinka, H Tamiya, T Murai, K Atagi, K Shimadzu, H Ujino, T Miyaichi, M Kan, A Kaji, K Haze**
*Emergency and Critical Care Medical Center, Osaka City General Hospital, Osaka, Japan*
*Critical Care* 2005, **9(Suppl 1):**P322 (DOI 10.1186/cc3385)

**Objective** The aim of our study was to investigate the prognostic factors in patients with cardio and/or respiratory failure who received percutaneous cardiopulmonary support (PCPS) therapy in the ICU.
**Materials and methods** The population was a total of 148 patients (105 adults, 13 children, 30 newborn infants) who received PCPS therapy from July 1994 to June 2004. We evaluated the patients' ages, clinical characteristics, the number of days of PCPS therapy, $PaO_2/FiO_2$, and hemodynamic parameters, including base excess at the time of discontinuing PCPS. We classified the cases into five groups considering the clinical characteristics: cardiac disease, non-cardiac disease including acute respiratory failure, postoperative cardiac failure, congenital heart disease and operation-assisted cases ($n = 58$, $n = 38$, $n = 18$, $n = 28$ and $n = 6$, respectively).
**Results** Seventy-three of the 148 patients could be taken off PCPS; however, 37 of those 73 patients died within 4 weeks after

removing the PCPS. The mortality was 76% (adults 78%, children 61%, newborn infants 90%). In 104 adult patients, those who required PCPS for more than 7 days exhibited significantly poor prognosis. In the five groups, mortality was 67%, 76%, 95%, 89% and 33%, respectively. Patients who had less than –2 on the base excess level and less than 200 on the $PaO_2/FiO_2$ level when the PCPS was removed had significantly poor prognoses.

**Conclusions** A low $PaO_2/FiO_2$, a low base excess and a long course of PCPS therapy are very poor prognostic indicators in patients receiving PCPS therapy. PCPS therapy has been proven effective in acute respiratory and cardiac failure cases, but we suggest that PCPS therapy has to be carefully limited considering all the clinical characteristics because the mortality rate is still so high.

## P323

### Practice of extracorporeal membrane oxygenation in adult patients: a single-centre experience

**R Tiruvoipati, S Chatterjee, C Harvey, G Faulkner, H Killer, A Sosnowski, R Firmin, G Peek**
*Glenfield Hospital, Leicester, UK*
*Critical Care* 2005, **9(Suppl 1):**P323 (DOI 10.1186/cc3386)

Extracorporeal membrane oxygenation (ECMO) is used as a treatment modality in patients with severe but potentially reversible cardiorespiratory failure that is not responding to conventional treatments. Practice of ECMO for neonatal respiratory failure has now become evidence-based practice supported by randomised controlled trials. Efficacy of ECMO in treating adult patients with severe respiratory failure is currently being investigated in a multicentre randomised controlled trial in the UK – the CESAR trial (www.cesar-trial.org). The aim of this study is to review the practice of ECMO in adult patients and to identify complications of ECMO associated with mortality.

This study is a retrospective review of case records, microfilms and our database between August 1989 and May 2004. All adult patients (aged 18 years or more) who received ECMO for severe respiratory failure at our hospital were included. The indication for use of ECMO in respiratory failure is a Murray score of more than 3 or a pH of less than 7.2 with uncompensated hypercapnoea not responsive to conventional ventilation. Venovenous ECMO was used in most of the patients with respiratory failure and venoarterial ECMO was used in patients with primary cardiac failure. Complications on ECMO were classified as mechanical (if the complication was related to the ECMO circuit used) or patient complications.

A total of 269 adult patients received ECMO in our unit. ECMO was used for respiratory failure in 94% (pneumonia 54.6%, primary ARDS 14.5%, secondary ARDS 8%, status asthamaticus 1.86% and other causes in 15% of patients) and cardiac failure in 6% of patients. Out of these, 42 patients were excluded from the analysis as they were part of the CESAR trial. The over all survival to discharge was 65%. Complete data on the complications were available in 222 out of 227 patients. The incidence of mechanical and patient-related complications were as follows.

Mechanical complications: clots in oxygenator 94 (42.3%), clots in bladder 55 (24.8%), oxygenator failure 51 (23.0%), clots in bridge 47 (21.2%), cracks on connectors 18 (8.1%), pump malfunction 15 (6.8%), cannula problems 13 (5.9%), race way/tubing rupture 4 (1.8%) and air in circuit 2 (0.9%).

Patient-related complications: cardiac failure requiring inotropes 115 (51.8%), renal 102 (45.9%), infections 60 (27.0%), arrhythmias 50 (22.5%), cannula site bleeding 32 (14.4%), metabolic 32 (14.4%), pulmonary 29 (13.1%), gastrointestinal haemorrhage 15 (6.8%), clinical brain death 8 (3.6%), hypertension requiring vasodilator therapy 6 (2.7%), cerebral infarction 2 (0.9%), and intra-cranial bleeding 2 (0.9%).

The mean number of complications is 3.06 (standard deviation 2.48) per patient. Multiple logistic regression analysis of these complications revealed cannulation site bleeding, hypertension, cardiac arrhythmias and pulmonary complications were independently associated with mortality and none of the mechanical complications were associated with mortality.

ECMO is a viable option in managing adult patients with severe but potentially reversible respiratory and cardiac failure. Mechanical complications of ECMO are not associated with mortality in such patients. This may be because of the expert care of the ECMO circuit by the dedicated ECMO specialists.

## P324

### Elevated plasma levels of troponin I in surgical patients: analysis of risk factors and outcomes

**M Alsahaf[1], H Barker[2]**
*[1]Kingston Hospital, Kingston Upon Thames, UK; [2]Royal Brompton Hospital, London, UK*
*Critical Care* 2005, **9(Suppl 1):**P324 (DOI 10.1186/cc3387)

A retrospective study of the application of troponin I assays in postoperative patients admitted to the intensive care and high dependency units in a busy district hospital was performed. Preoperative patient demographics and cardiac risk factors, prior medical history and type and urgency of surgery were correlated with the results of troponin assays: only patient gender was significantly associated, with more females having elevated serum troponin I. Outcomes were worse when troponin I was raised, with a significantly higher mortality and trend to more organ systems failed. The study was limited by small size (47 patients) and non-standardisation of the timing of troponin assay after admission. A larger prospective study needs to be performed with assays at agreed time or trigger points.

The patient cohort was derived from admissions to the ICU or high dependency units (HDU) in a busy district general hospital during a 9-month period from January to September 2003. Data were collected retrospectively from the biochemistry laboratory database in order to identify those patients whose troponin I levels were assayed during this period.

Serum troponin I was measured in 61 patients in the ICU or HDU setting. Of these, 14 were medical patients with myocardial infarction and were excluded from the study. The other 47 patients were surgical and they form the cohort for this study. Patients whose serum troponin was measured comprised 31 males and 16 females. Their mean age was 74 years (range 49–93, standard deviation [SD] 10 years).

Among the 47 patients in whom a suspicion of myocardial dysfunction had precipitated the laboratory test, 36 had abnormally high serum levels of troponin I (troponin I $>0.05$ units in our laboratory). In none of these cases had there been any demonstration of myocardial infarction on electrocardiography nor echocardiography. The remaining 11 patients were classified as having normal troponin I levels and no biochemical evidence of myocardial injury.

All the patients in the normal troponin group were male, but the other cohort comprised 16 females and 20 males. This was a significant difference in sex distribution ($P=0.006$, chi-squared test) (Table 1).

Analysing the outcomes of patients with raised troponin levels compared with those with normal values (summarised in Table 2), the presence of an elevated serum troponin I was associated with a shorter duration of stay although this did not reach statistical

**Table 1 (abstract P324)**

| | Total (mean ± SD) | Normal TI (mean ± SD) | Raised TI (mean ± SD) | Normal TI vs raised TI |
|---|---|---|---|---|
| Urgency score (1–3) | 1.9 ± 1.3 | 2.2 ± 0.4 | 2.1 ± 0.8 | $P = 0.88$ |
| Previous cardiac Hx (0–2) | 0.4 ± 0.5 | 0.5 ± 0.7 | 0.4 ± 0.5 | $P = 0.58$ |
| Number of cardiac meds | 1.4 ± 1.5 | 1.1 ± 1.9 | 1.5 ± 1.4 | $P = 0.81$ |

**Table 2 (abstract P324)**

| | Total (mean ± SD) | Normal TI (mean ± SD) | Raised TI (mean ± SD) | Normal TI vs raised TI |
|---|---|---|---|---|
| Length of stay | 13 ± 18.3 | 22 ± 30 | 10.5 ± 12.1 | $P = 0.12$ |
| Number of organs failed | 1.9 ± 1.2 | 1.5 ± 1.4 | 2.0 ± 1.2 | $P = 0.35$ |
| Dead | 15/47 | 2/11 | 13/36 | $P < 0.0005$ |

significance ($P = 0.12$, unpaired $t$ test). This contrasts with their having more organ failure as already defined: cases with abnormal serum troponin I levels had a mean of 2.0 organ systems fail during their stay in ICU/HDU, compared with 1.5 organ systems in the normal troponin I group. However, the apparent difference between the groups in numbers of organs failed did not achieve significance ($P = 0.35$, $t$ test).

Among those with normal troponin tests, two of 11 patients died. This was a lower proportion than in the group with elevated serum troponin levels, in whom 13 of 36 patients died. This was statistically a highly significant difference ($P < 0.001$, chi-squared analysis).

## P325

### Prognostic value of serum troponin levels in patients with pulmonary embolism: a systematic review and meta-analysis

**J Latour Pérez[1], E Palencia Herrejón[2], F Gordo Vidal[3], B Sánchez Artola[4]**

*[1]Hospital General de Elche, Alicante, Spain; [2]Hospital Gregorio Marañón, Madrid, Spain; [3]Fundación Hospital de Alcorcón, Madrid, Spain; [4]Hospital Gómez Ulla, Madrid, Spain*

*Critical Care* 2005, **9(Suppl 1):**P325 (DOI 10.1186/cc3388)

**Objective** Patients with pulmonary embolism (PE) often show elevated plasmatic troponin levels; this condition may be associated with increased mortality and other adverse outcomes. To clarify the possible association between serum troponin levels and clinical outcome in patients with PE we performed a systematic review of the literature.

**Data source** The search strategy included electronic search of original studies in Medline, Embase, Cochrane Library, Pascal, Medion and ISI Proceedings, manual retrieval of recovered bibliographic references and personal communication with authors.

**Study selection** We selected inceptive cohort studies relating baseline troponin levels and the occurrence of hospital mortality, unfavourable clinical course or echocardiographic signs of right ventricular dysfunction. The reviewers screened the articles independently for eligibility and resolved disagreements by consensus.

**Extraction, quality assessment and results** Data about odds ratio (OR), sensitivity, specificity, likelihood ratios (LR) with confidence interval (95% CI), study population, type of test assay used (troponin T or troponin I), and methodological quality (using a modified score after the Lijmer and Altman checklist) were obtained independently in a duplicate form and disagreements resolved by consensus. Concordance between reviewers was assessed using the weighted kappa statistic. We explored methodological, statistical and clinical heterogeneity, and built a meta-regression model to explore threshold effects, constructed the Summary Receiver Operating Characteristic (SROC) curves and quantified the impact of study's characteristics on the magnitude of effects, using StatsDirect (v 2.3.7), SPSS (v 11.0.1) and Meta-Disc (v 1.1.0) software.

**Results** We identified 13 studies, which included 1293 patients. Agreement for quality assessment previous to consensus for each pair of reviewers were 0.51 (95% CI 0.30, 0.72) and 0.74 (95% CI 0.58, 0.90), respectively. The quality of recovered studies was not optimal. The studies were relatively homogeneous for each outcome, and there was no evidence of threshold effect or publication bias. Overall weighted mortality was 14%. The presence of high troponin levels identified a subgroup of patients at high risk of: dying during the hospitalization (OR 6.20 [95% CI 4.04, 9.52]; area under SROC curve [AUC] 0.78 [CI 95% 0.73, 0.83]), showing echocardiographic signs of right ventricular dysfunction (OR 8.04 [95% CI 4.40, 16.69]; AUC 0.80 [95% CI 0,77, 0,82]), and suffering an unfavourable clinical course (OR 14.58 [95% CI 6.82, 31.16]; AUC 0.84 [95% CI 0.75, 0.94]). Normal troponin levels identified patients with favourable clinical course (LR 0.23 [95% CI 0.13, 0.41]).

**Conclusions** Troponin levels are useful to stratify the risk in patients with PE. In the individual patient, normal troponin levels indicate a high probability of following a favourable clinical course.

## P326

### Pulmonary embolism in younger and older adults: clinical presentation and comparison of right ventricular dysfunction, a new prognostic echocardiographic index

**N Parenti, S Bonarelli, A Fanciulli**

*M. Bufalini, Cesena, Italy*

*Critical Care* 2005, **9(Suppl 1):**P326 (DOI 10.1186/cc3389)

**Introduction** Previous reports suggested that clinical presentation of pulmonary embolism (PE) could be different in younger as compared with older patients and the presence of right ventricular dysfunction (RVD) at echocardiography could identify a group of PE patients with poor short-term prognosis. We tested these hypotheses and compared in these two groups a new prognostic echocardiographic index: the RVD.

**Methods** This is an observational retrospective study of 80 consecutive patients (40 younger, age ≤ 45 years; 40 older, age > 45 years) admitted to the ED of an urban hospital from January 1996 to June 2003 for suspected PE, confirmed by high-probability lung scan and/or spiral CT. All patients had symptomatic PE and SBP ≥ 100 mmHg at presentation. A 2D

transthoracic echocardiogram was performed on all patients within 24 hours of diagnosis of PE. The severity of PE was based on the number of non-perfused pulmonary segments on lung scan or spiral CT. We excluded patients with severe COPD, shock/hypotension (SBP <100 mmHg) and/or chronic pulmonary hypertension. We collected data of history, symptoms, signs, laboratory, chest X-ray, ECG and echocardiographic findings. RVD diagnosis was made with echocardiography, in the presence of right/left ventricular end-diastolic diameter ratio > 0.7 in the parasternal long axis view without RV hypertrophy. We used the Student *t* test or Fisher's exact test to compare the two groups.

**Results** Mean ages were 39 years (range 25–45 years) for younger and 81 years (range 70–93 years) for older adults. After comparison with older patients, younger patients had less typical PE risk factors (in particular recent immobilization: 20% vs 35%, $P = 0.03$; malignancy: 6% vs 36%, $P < 0.001$); less abnormal ECG: 40% vs 70%, $P < 0.001$ (right BBB was the more frequent abnormality in younger adults 30% vs 17%, $P < 0.001$); less abnormal X-ray (20% vs 40%, $P < 0.001$); lower D-dimer levels: mean of 875.8 μg/l vs 1889.7 μg/l in older adults ($P < 0.05$). Among younger adults, the more frequent symptoms were: dyspnoea (50%), chest pain (50% vs 30% in older, $P = 0.006$), cough (20% vs 5% in older, $P = 0.003$), hemoptysis (15% vs 5%, $P < 0.03$). At presentation, younger patients showed better parameters, better air room ABG ($PaO_2$, oxygen alveolar–arterial difference). Two groups had similar severity of PE: mean of non-perfused segments: $7.9 \pm 3.1$ standard deviation for younger patients vs $9.2 \pm 5.9$ standard deviation for older patients ($P = 0.38$). In two groups the number of patients with RVD was very similar: 32.5% in older adults vs 30% in younger ($P > 0.05$).

**Discussion** Our study indicates that PE may present more subtly among younger patients. These results could be explained by the different pathophysiology and compensation of PE in younger patients. To our knowledge no one has compared the RVD in these two groups. Because of different pathophysiology and compensation of PE in these two groups, we were surprised to find a similar rate of RVD. Maybe the acute onset of PE does not allow compensation in both populations. The main limitations of the study were: few patients, incomplete data on etiology of PE in younger patients (few laboratory tests on thrombophilias), and the retrospective design of the study.

**Conclusion** This study suggests one should be careful of insidious presentations of PE in younger patients and that RVD, a novel prognostic echocardiographic index, could be used in younger patients as in older patients.

## P327

### Pulmonary embolism originated from right heart chamber thrombus: the diagnostic role of transesophageal echocardiography

**B Volgyes, M Mezei, R Szücs, A Tóth**
*Bajcsy Zs kh, Budapest, Hungary*
*Critical Care* 2005, **9(Suppl 1):**P327 (DOI 10.1186/cc3390)

**Background** Pulmonary embolism (PE) usually arises from the thrombi originating in the deep venous system of the lower extremities, pelvic or renal vein; however, it may rarely originate in the upper extremity veins and the right heart chambers. Ninety per cent of all pulmonary emboli arise from the deep venous system, usually from the lower extremities. In symptomatic patients, venous ultrasonography has a sensitivity of 95%, a specificity of 96%, a positive predictive value of 97%, and a negative predictive value of 98%. Rarely the source of emboli may be the right atrium, or the thrombi stagnate in the right heart chambers. Transthoracic or transesophageal echocardiography may directly visualize embolized thrombi (right heart chambers or central pulmonary arteries). The incidence of PE is 0.5–1/1000 cases.

**Materials and methods** Eleven patients with massive pulmonary embolism, age 36–91 (median 72) years, were treated in the ICU between January 2001 and July 2004. Searching for the source of embolism, venous ultrasonography of lower extremities and transesophageal echocardiography (TEE) were performed. The right heart chambers thrombus could be visualized with TEE; distal embolization of the thrombus into the pulmonary vasculature was suspected. The first and conclusive examination of massive PE is TEE. The presence of intracardial thrombus was enough in itself to indicate thrombolysis therapy. Eleven patients were treated in our study with massive PE. All the patients received tissue plasminogen activator (rt-PA), 100 mg over 2 hours, and continuous echocardiographic monitoring demonstrated clot dissolution within 1 hour in all patients.

**Results** There was no re-embolism into the pulmonary vessels during the thrombolysis. There was in one case moderate haemorrhagic complication. One patient died in PE because of the insufficiency of thrombolysis. Nine patients out of 11 should have treated mechanical ventilation. Ten patients were discharged.

**Conclusions** Due to the low number of patients our statements are tendency and nondescript. The right heart chamber thromboses verified by TEE are effectively treated with rt-PA. Based on our opinion the lysis activity of rt-PA was faster and more effective than the treatment of streptokinase.

## P328

### The use of type brain natriuretic peptide in a cardiac surgery postoperative context

**A Rouge, RV Gomes, P Nogueira, M Fernandes, C Karam, C Rutherford, L Pinto Carvalho, L Campos, H Rocha Dohmann**
*Pró-Cardíaco, Rio de Janeiro, Brazil*
*Critical Care* 2005, **9(Suppl 1):**P328 (DOI 10.1186/cc3391)

**Background** Several scientific publications have shown the importance of the brain natriuretic peptide (BNP).

**Objective** To evaluate the BNP kinetics and its correlation with oxyhemodynamic variables at the postoperative (PO) stage of cardiac surgery (CS).

**Methods** A classical cohort was carried out with 22 patients undergoing CS, who were consecutively selected from August 2003 to January 2004. The mean age of the patients was $65.7 \pm 8.18$ years, and three were females (13.6%). The type B BNP was dosed before (Pre-BP), at the first hour (BNP 1) and the sixth hour (BNP 6) PO. The laboratory and hemodynamic data were also registered. The quantitative dosage of BNP was done by the immunofluorescence method (Biosite Triage BNP test). The results underwent statistical analysis with the following tests: chi-square, Student *t*, Mann–Whitney, and Pearson, followed by logistic regression and stepwise (likelihood ratio).

**Results** No significant difference among Pre-BNP and BNP 1 was found ($P = 0.84$), but the opposite occurred when comparing pre-BNP and BNP6 ($P = 0.0004$). BNP 1 was significantly related to the first hour PAM (PAM 1), $P = 0.023$; with the (DELTAPP), $P = 0.292$; Spearman rho = 0.475913, which produced the possible correlation equations: PAM 1 hour = (89.8432 + 0.0356) × BNP and DELTAPP = (12.7283 – 0.0087) × BNP. There was no correlation between the use of VA (dobutamine or noradrenaline) and the BNP 1 and BNP 6. The MODS was correlated to BNP 6 ($P = 0.01$ and rho = 0.524) but no significant correlation between the BNP 1 and the PO evaluated variables was found. The BNP 1, BNP 6 and the BNP were not able to

predict a longer length of stay in the surgical ICU or greater MODS at the third day.
**Conclusion** Preliminary data show a BNP kintetics curve at PO CS, as well as a linear correlation among BNP 1 and PAM 1 hour and DELTAPP and BNP 6. The MODS score was correlated to BNP 6. The noncorrelation with the outcome variables may be related to the sample size.

### P329

### Pro-B-type natriuretic peptide predicts mortality in critically ill patients

**B Meyer, M Huelsmann, G Delle Karth, P Wexberg, O Wagner, G Heinz**
*Medical University of Vienna, Austria*
*Critical Care* 2005, **9(Suppl 1):**P329 (DOI 10.1186/cc3392)

**Background** Natriuretic peptides have emerged during recent years as potent prognostic markers in patients with heart failure and other cardiovascular diseases. Moreover, natriuretic peptides show strong predictive value in patients with pulmonary embolism, sepsis and renal failure. Also, first data imply that BNP is a good predictor of outcome in a selected population (shock) of critically ill patients.
**Aim** To test the hypothesis that N-terminal pro-B-type natriuretic peptide (pro-BNP) serves as a prognostic marker in an unselected cohort of intensive care patients.
**Design** A prospective, observational study at a tertiary ICU.
**Methods** Eighty-one consecutive patients (age 63 ± 16 years, male $n = 51$, SAPS 2 score 49 ± 11, mechanical ventilation $n = 50$, vasopressors $n = 56$, renal failure $n = 19$, postoperative $n = 23$) admitted to the ICU during a 3-month period were evaluated. Plasma samples of all patients were obtained upon ICU admission. Pro-BNP was determined using commercially available kits (Roche Diagnostics). Subgroup analyses comprised main diagnosis (cardiologic/non-cardiologic and medical/postsurgery) and presence and category of shock. Data were compared after logarithmic transformation.
**Results** Pro-BNP levels were significantly higher in patients who died ($n = 17$) than in ICU survivors (13,871 ± 19,869 vs 5304 ± 8211 pg/ml, $n = 17$ vs $n = 64$, $P = 0.02$). There was no significant difference in pro-BNP between cardiologic and other medical patients (9794 ± 14,379 vs 7099 ± 11,208, $P = 0.91$) but pro-BNP was significantly lower in postoperative patients (3671 ± 6600 vs 9131 ± 14,090 pg/ml, $P = 0.045$, surgical and medical patients, respectively). Patients presenting with shock showed significantly higher levels of pro-BNP (14,321 ± 17,653 vs 5264 ± 8605 pg/ml, $P < 0.001$); however, no difference was observed between cardiogenic and septic shock categories.
**Conclusion** Pro-BNP might be a strong predictor of outcome even in an unselected population of critically ill patients.

### P330

### Elevated N-terminal pro-B-type natriuretic peptide levels and normal left ventricular systolic function: an echocardiographic study

**A Turley, B Kunadian, A Roberts, A Davies, M de Belder, J Drury, M Stewart**
*James Cook University Hospital, Middlesbrough, UK*
*Critical Care* 2005, **9(Suppl 1):**P330 (DOI 10.1186/cc3393)

**Introduction** The neurohormone N-terminal pro-B-type natriuretic peptide (NT-proBNP) has been shown to be a useful 'rule-out' test for the diagnosis of left ventricular systolic dysfunction (LVSD). As NT-proBNP plasma levels are related to left ventricular wall tension, NT-proBNP may be elevated in the absence of LVSD.
**Aim** To evaluate echocardiographic abnormalities in patients with elevated levels of NT-proBNP and clinical symptoms and signs suggestive of LVSD but with normal LV systolic function on echocardiography.
**Methods** Within two primary care trusts, NT-proBNP was measured in 1054 patients over a 1-year period (September 2003–October 2004). To assess echocardiographic abnormalities other than LVSD we retrospectively reviewed our digital archive database.
**Results** NT-proBNP was elevated (>150 ng/l) in 744/1054 patients (70.6%), 42% male, median age 76 years (33–100 years). Of those patients with an elevated NT-proBNP 492/744 (66%) had an echocardiogram. A cut-off value of 150 ng/l was used, sensitivity 0.97 (confidence interval [CI] 0.94–0.98), specificity 0.45 (CI 0.41–0.48), positive predictive value 0.44 (CI 0.41–0.48), negative predictive value 0.97 (CI 0.94–0.98).
Three hundred and twenty-eight patients had normal LV systolic function and an elevated NT-proBNP. Of these, echocardiographic abnormalities were seen in 252/328 (77%). These included LVH 152/328 (46%), aortic stenosis 19/328 (6%), aortic regurgitation 48/328 (15%), mitral stenosis 11/328 (3%), mitral regurgitation 104/328 (32%), tricuspid regurgitation 80/328 (24%) with significant pulmonary hypertension in 57/328 (17%), and 14 patients had a previous valve replacement. A significant pericardial effusion was found in two patients.
**Conclusion** NT-proBNP is a useful tool in the 'rule-out' of LVSD. When elevated, many clinically relevant pathologies other than LVSD may be identified.

### P331

### N-terminal pro-B-type natriuretic peptide and the diagnosis of left ventricular systolic dysfunction: what is the optimal cut-off?

**A Turley, A Roberts, B Kunadian, A Davies, M de Belder, J Drury, M Stewart**
*James Cook University Hospital, Middlesbrough, UK*
*Critical Care* 2005, **9(Suppl 1):**P331 (DOI 10.1186/cc3394)

**Introduction** The neurohormone N-terminal pro-B-type natriuretic peptide (NT-proBNP) is predominantly released from the left ventricle in response to increasing wall tension, and is suggested as a useful screening test for suspected left ventricular systolic dysfunction (LVSD).
**Aim** To evaluate the predictive value of different NT-proBNP reference cut-off values in patients with clinical symptoms and signs suggestive of LVSD.
**Methods** NT-proBNP was measured in 1054 patients with clinical symptoms and signs suggestive of LVSD over a 1-year period (September 2003–October 2004). We retrospectively reviewed our digital archive echocardiographic database.
**Results** An echocardiogram was performed in 549/1054 (52%) patients. NT-proBNP was >150 ng/l in 744/1054 patients (71%), 42% male, median age 76 years (33–100 years) and > 500 ng/l in 411/1054 patients (40%), 50% male, median age 76 years (33–100 years). ROC curves are shown for NT-proBNP cut-off values of 150 ng/l, positive predictive value (PPV) 0.22 (confidence interval [CI] 0.19–0.25), negative predictive value (NPV) 0.97 (CI 0.94–0.98), and 500 ng/l, PPV 0.3 (CI 0.26–0.35), NPV 0.93 (CI 0.9–0.94), for the detection of LVSD.
At a cut-off value of 500 ng/l, NT-proBNP has a sensitivity 0.85 (CI 0.76–0.91), specificity 0.67 (CI 0.64–0.69), PPV 0.18 (CI 0.15–0.22), and NPV 0.98 (CI 0.97–0.99) at detecting moderate to severe LV impairment.

**Figure 1 (abstract P331)**

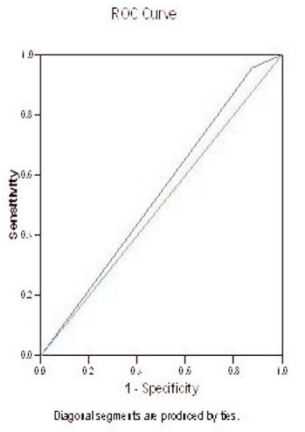
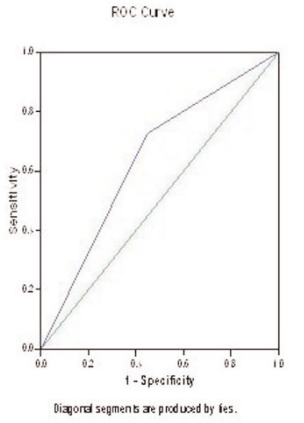



**Figure 2 (abstract P331)**




**Conclusion** NT-proBNP is a useful tool in the 'rule-out' of LVSD. An NT-proBNP level of 500 ng/l has a similar negative predictive value to an NT-proBNP level of 150 ng/l with improved positive predictive value. This is particularly important in this population where other confounding comorbidities are common.

### P332

### Pro-atrial natriuretic peptide in patients with sepsis, severe sepsis and septic shock

**M Prucha[1], R Zazula[2], I Herold[3], M Dostal[4], B Kavka[1]**
*[1]Hospital Na Homolce, Prague, Czech Republic; [2]Thomayer's Hospital, Prague, Czech Republic; [3]Klaudian´s Hospital, Mlada Boleslav, Czech Republic; [4]Institute of Experimental Medicine, Prague, Czech Republic*
*Critical Care* 2005, **9(Suppl 1):**P332 (DOI 10.1186/cc3395)

**Introduction** The natriuretic peptides are counter-regulatory hormones involved in volume homeostasis and cardiovascular remodeling. Both ANP and BNP are released by the heart in response to several stimuli, the most prominent of which being increased intravascular volume and increased intraventricular pressure. Recently, interest has focused on their significance in patients with sepsis and septic shock. A correlation between ANP and IL-6 was found in patients with septic shock [1].
**Objectives** The present study aimed at examining: serum levels of the stable midregional prohormone forms of ANP in patients with sepsis, severe sepsis and septic shock; and correlations of proANP with cytokines involved in the pathogenesis of the sepsis.
**Patients and methods** Serum concentrations of proANP were determined using the immunoluminometric assay in 17 consecutive patients admitted to the medical intensive care unit for sepsis (two patients) severe sepsis (five patients) and septic shock (10 patients). ProANP levels as well as those of procalcitonin, IL-6, IL-10 and lipopolysaccharide binding protein were measured at day 1 and in the course of the stay at the intensive care unit. ProANP was also determined in 12 healthy adults.
**Results** The median APACHE II score of surviving patients was 18; minimum 5, maximum 25; of non-survivors median APACHE II score was 22.5; minimum 5, maximum 31 on day 1. Eight of the 17 patients died (47%). Significantly higher concentrations ($P = 0.001$) of proANP were measured in survivors (412.1 pmol/l; minimum 89; maximum 1486.1) and non-survivors (447.5 pmol/l; minimum 201.8; maximum 1876) as compared with controls (50.7 pmol/l; minimum 33.4; maximum 64.5). Significantly higher concentrations (733.8 pmol/l; minimum 201.8; maximum 1876) of proANP were in patients with severe sepsis and septic shock as compared with patients with sepsis (399.9 pmol/l; minimum 89; maximum 897), $P = 0.0053$. There were no differences of proANP levels between survivors and non-survivors. There was no significant correlation between proANP and cytokine levels measured simultaneously.
**Conclusions** ProANP levels are elevated in the course of sepsis, severe sepsis and septic shock. The ANP levels do not correlate with the levels of PCT, IL-6, IL-10, LBP.
**Reference**
1. *Intensive Care Med* 2003, **29:**1696-1702.

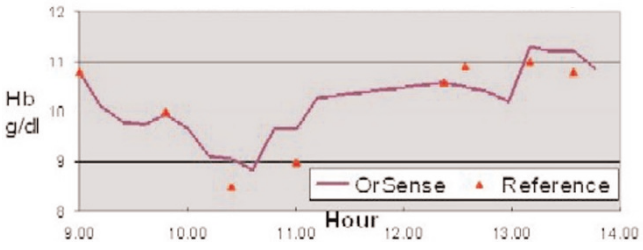
### P333

### Evaluation of a noninvasive hemoglobin and hematocrit monitoring device

**D Dvir[1], D Geva[2], O Amir[1], I Fine[1], E Monashkin[1], G Fostick[1], E Segal[3]**
*[1]Orsense, Rehovot, Israel; [2]Kaplan Medical Center, Rehovot, Israel; [3]ICU Sheba Medical Center and OrSense Affiliation, Ramat Gan, Israel*
*Critical Care* 2005, **9(Suppl 1):**P333 (DOI 10.1186/cc3396)

**Introduction** Optimal monitoring of critically ill patients remains a challenge. A noninvasive point-of-care test of blood hemoglobin and hematocrit (Hb/Hct) levels may provide rapid patient assessment, including the need for transfusion, less iatrogenic blood loss and cost savings. A new, noninvasive device, the OrSense NBM-100, was tested for continuous monitoring (CM) of Hb/Hct in an ICU and postanesthesia care unit (PACU).
**Objective** The aim of this study was to evaluate the accuracy of a new noninvasive Hb/Hct continuous monitor, compared with the traditional laboratory technique in critically ill and postsurgery patients.
**Materials and methods** The NBM-100 device utilizes a finger-base ring-like sensor using red–near infrared occlusion spectroscopy to detect and analyze the Hb/Hct concentrations and blood glucose level.
**Study design** Ten patients were enrolled (four females, six males, ages 24–83): four in the PACU, and six in the ICU. The NBM-100 probe was placed on patients' thumbs and assessed for 2–12 hours of CM. NBM-100 output was provided every 10–15 min. Results of the device were compared with arterial blood samples taken every 30–60 min and analyzed by blood gas machine (Nova Biomedical).
**Results** The NBM-100 showed Hb trend tracking for 54 hours of CM (see for example Fig. 1). The mean absolute error was 1.0 g/dl (84 points, Hb range: 8.5–12.6 g/dl). An average bias of 0.3 g/dl was

**Figure 1 (abstract P333)**




NBM-100 hemoglobin (Hb) tracking versus spot Hb values in one patient when calibrated with the first *in vitro* measurement.

found between the two methods. When calibrated with the input of the first *in vitro* measurement, the mean absolute error was 0.95 g/dl.

**Conclusions** The OrSense monitor can provide accurate, noninvasive Hb CM in critically ill patients. This may be useful for diagnosis and treatment of patients with significant Hb changes. The device and sensor provided the capability of long-term CM and early-trend information at the point of care. Particularly, the device could be valuable in patients with wide Hb dynamic ranges resulting from blood dilution and hemorrhaging.

Preliminary results of ongoing trials evaluating the NBM-100 in other settings (e.g. intermittent Hb/Hct measurements in hematology clinics and in blood banks) show a good agreement between NBM-100 and standard invasive Hb/Hct measurement methods. Further developments may enable noninvasive measurement of glucose as well.

## P334

## Hematocrit of 20% versus 25% during normothermic cardiopulmonary bypass for elective coronary artery bypass graft surgery

**C von Heymann, M Sander, A Foer, A Heinemann, J Braun, P Dohmen, W Konertz, C Spies**
*University Hospital Charité, Berlin, Germany*
*Critical Care* 2005, **9(Suppl 1):**P334 (DOI 10.1186/cc3397)

**Introduction** Much debate still exists on the minimum level of normovolemic hemodilutional anemia that is safe to maintain oxygen delivery within the physiological range [1]. Normothermia during cardiopulmonary bypass (CPB) raises the question of adequate regional and whole body oxygen delivery under conditions of hemodilutional anemia [2]. We performed a prospective, controlled and randomized study to investigate oxygen delivery, oxygen consumption and clinical outcome of patients who were randomly allocated to a hematocrit of 20% or 25%, respectively, during normothermic cardiopulmonary bypass for isolated CABG surgery.

**Patients and methods** After approval of the local ethical committee and informed written consent 50 patients were randomized to a hematocrit of $20 \pm 1\%$ versus $25 \pm 1\%$ during normothermic CPB. Inclusion criteria were: informed consent, isolated CABG surgery, age >18 and < 75 years, Hct > 36% and bodyweight > 70 kg. Prior to CPB patients were subjected to isovolemic hemodilution using HES130/0.4 (Voluven, Fresenius, Germany). Outcome measures of this study were: blood lactate, postoperative drainage loss and transfusion requirements, incidence of organ dysfunction (neurological, cardiac, respiratory and renal), stay in ICU (hours) and hospital stay (days). Postoperative intensive care therapy followed a standardized protocol. Statistical analysis was performed using the chi-squared test and Fisher's exact test for categorical and dichotomous variables, respectively. The Mann–Whitney U test was applied for intergroup comparison of continuous variables.

**Results** One patient had to be excluded from statistical analysis due to clot formation in the autologous blood that had to be discarded. Basic patient characteristics are presented in Table 1,

**Table 1 (abstract P334)**

**Basic patient characteristics**

| | Hematocrit 25% | | Hematocrit 20% | | |
|---|---|---|---|---|---|
| | Median | IQR | Median | IQR | *P* |
| Age (years) | 60 | 56–67 | 64 | 58–71 | 0.28 |
| Gender (male/female) | 25/2 | | 22/0 | | 0.50 |
| Body mass index (kg/m$^2$) | 28.1 | 26.1–32.6 | 28.6 | 25.2–29.4 | 0.36 |
| Preoperative hematocrit (%) | 41.8 | 40.2–43.0 | 41.9 | 39.4–43.4 | 0.92 |
| Duration of anesthesia (min) | 300 | 285–320 | 305 | 290–325 | 0.28 |
| Duration of surgery (min) | 195 | 160–220 | 205 | 175–250 | 0.15 |
| CPB time (min) | 70 | 52–82 | 73 | 65–81 | 0.40 |
| Cross-clamp time (min) | 45 | 32–57 | 45 | 38–49 | 0.72 |
| APACHE II score | 14 | 11–19 | 17 | 12–20 | 0.18 |

**Table 2 (abstract P334)**

**Outcome variables**

| | Hematocrit 25% | | Hematocrit 20% | | |
|---|---|---|---|---|---|
| | Median | IQR | Median | IQR | *P* |
| Hematocrit on admission to ICU (%) | 25.8 | 24.0–26.9 | 23.5 | 20.8–25.3 | 0.04 |
| $DO_2$ on admission to ICU (ml/m$^2$/min) | 819 | 675–1089 | 787 | 665–948 | 0.43 |
| $VO_2$ on admission to ICU (ml/m$^2$/min) | 227 | 190–289 | 211 | 185–263 | 0.78 |
| $DO_2$ 18 hours after admission to ICU (ml/m$^2$/min) | 991 | 743–1299 | 910 | 807–1032 | 0.66 |
| $VO_2$ 18 hours after admission to ICU (ml/m$^2$/min) | 327 | 269–399 | 285 | 265–347 | 0.16 |
| Blood lactate on admission to ICU (mmol/l) | 1.4 | 1.1–2.1 | 1.4 | 1.1–2.0 | 0.95 |
| Blood lactate 18 hours after admission to ICU (mmol/l) | 1.4 | 1.1–2.1 | 1.8 | 1.2–2.2 | 0.69 |
| Drainage loss (ml) | 390 | 280–470 | 400 | 270–580 | 0.88 |
| Transfused patients (*n*) | 0 | 0% | 2 | 9% | 0.51 |
| Agitated arousal reaction (*n*) | 3 | 13% | 3 | 14% | 0.59 |
| Myocardial infarction (*n*) | 0 | 0% | 0 | 0% | 0.99 |
| CK/CK-MB | 0.05 | 0.04–0.07 | 0.05 | 0.04–0.08 | 0.99 |
| Ventilator support (hours) | 10 | 7–13 | 10 | 9–12 | 0.74 |
| Creatinine 18 hours after admission to ICU (mg/dl) | 0.86 | 0.80–1.08 | 1.02 | 0.82–1.13 | 0.65 |
| Patients with acute renal failure (*n*) | 1 | 4% | 1 | 5% | 0.73 |
| ICU stay (hours) | 23 | 22–25 | 23 | 21–35 | 0.87 |
| Mortality (*n*) | 0 | 0% | 1 | 5% | 0.47 |

showing no significant differences between groups. Patients were discharged from the ICU after a median 23 hours in both groups ($P = 0.87$). Outcome variables were not significantly different between groups (Table 2) and within the normal range. Duration of hospital stay was not different between groups. One patient in the 20% group died of septic multiorgan failure due to pneumonia occurring on day 3 after surgery.

**Conclusion** The results of our study showed that whole body oxygen delivery was sufficiently maintained as blood lactate levels were not different between groups. Clinical outcome after elective CABG surgery was not impaired by an hematocrit of 20% during normothermic CPB. Furthermore, lowering the safe degree of hemodilutional anemia during CPB may prevent patients being exposed to blood products.

**References**

1. DeFoe GR: *Ann Thorac Surg* 2001, **71:**769-776.
2. Warm Heart Investigators: *Lancet* 1994, **343:**559-563.

## P335

### Anaemia at discharge from the intensive care unit is associated with an inappropriate erythropoietin response

**A Bateman, G Mills, T Walsh**
*Royal Infirmary of Edinburgh, UK*
*Critical Care* 2005, **9(Suppl 1):**P335 (DOI 10.1186/cc3398)

**Background and objectives** The adoption of a restrictive transfusion practice in our unit has led to a high prevalence of significant anaemia during the ICU stay, which persists to level 3 (L3) discharge. There has been little research exploring the recovery of anaemia following critical illness. We investigated the aetiology of the anaemia in patients at discharge from intensive care.

**Setting and patients** An 18-bed general intensive care unit within a tertiary hospital. Patients who required > 48 hours L3 care and were anaemic at time of L3 discharge were recruited. Exclusion occurred if renal replacement therapy or immunosuppression was required at time of discharge, or if patients had a chronic haematological abnormality.

**Methods** Haemoglobin (Hb) and erythropoietin (EPO) levels were measured within 5 days of L3 discharge, along with the percentage of hypochromic red cells (%HYPO), reticulocyte haemoglobin content (CHr), reticulocyte count, ferritin and vitamin B12 and folate levels.

**Baseline characteristics** Presented as median (first and third quartiles); range. Twenty male and 10 female patients were recruited with the following characteristics: age: 66.5 years (55.5, 77); 35–83. APACHE II score 21 (16, 24); 7–38. ICU length of stay (LOS): 12 days (9, 23.25); 2–46.

**Results** Data are presented in Table 1.

**Table 1**

| Parameter (normal value) | Median (first quartile–third quartile) | Range (minimum–maximum) |
|---|---|---|
| Hb (g/l) (>120) | 92.0 (87.7–100.2) | 78.0–120.0 |
| EPO (mIU/ml) (< 55) | 18.2 (9.1–25.9) | 4.3–83.4 |
| CHretic (pg) (> 28) | 32 (30.2–33.8) | 27.0–37.2 |
| %HYPO (< 5%) | 4.15 (2.2–6.9) | 0.7–19.7 |
| Reticulocyte × $10^9$ | 107.2 (75.1–145.2) | 47.1–331.3 |
| Vitamin B12 (ng/l) (>170) | 610 (416–1282) | 203–1827 |
| Folate (μg/l) (> 2) | 5.7 (3.6–7.5) | 2.3–12.6 |

**Conclusions** Anaemia persisting at ICU discharge is associated with an inappropriate EPO response in the majority of patients. The elevated reticulocyte count suggests that the erythropoietic response has been initiated despite low EPO levels but this is inadequate to correct anaemia. There is no evidence of vitamin B12 or folate deficiency. The normal CHr suggests little evidence of current functional iron deficiency but the elevated %HYPO in 40% of patients suggests that depleted iron stores may have limited erythropoiesis at some point during the ICU stay. Further work is required to determine factors contributing to the inappropriate EPO response.

## P336

### Recombinant human erythropoietin therapy in critically ill patients

**D Georgopoulos[1], D Matamis[2], N Xirouchaki[1], C Routsi[3], A Michalopoulos[4], A Maggina[5], G Dimopoulos[6], E Zakynthinos[7], G Nakos[8], G Thomopoulos[9], K Mandragos[10], G Vasiliadou[11], M Peftoulidou[12], A Maniati[13]**
*[1]University Hospital, Heraklion, Greece; [2]Papageorgiou Hospital, Thessaloniki, Greece; [3]Evagelismos University Hospital, Athens, Greece; [4]H Dunan Hospital, Athens, Greece; [5]Saint Olga Hospital, Athens, Greece; [6]Sotiria Hospital, Athens, Greece; [7]University Hospital, Larisa, Greece; [8]University Hospital, Ioannina, Greece; [9]Laiko Hospital, Athens, Greece; [10]Hellenic Red Cross Hospital, Athens, Greece; [11]Papanikolaou Hospital, Thessaloniki, Greece; [12]AHEPA University Hospital, Thessaloniki, Greece; [13]University Hospital, Patras, Greece*
*Critical Care* 2005, **9(Suppl 1):**P336 (DOI 10.1186/cc3399)

**Objective** The aim of our study was to assess the efficacy of two dosing schedules of recombinant human erythropoietin (rHuEPO) in increasing hemoglobin (Hb) level and reducing the exposure to allogeneic red blood cells (RBC) transfusion in critically ill patients.

**Design** A prospective, randomized, multicenter trial.

**Settings** A total of 13 intensive care units participated in the study.

**Patients** A total of 148 patients who met eligibility criteria were enrolled.

**Intervention** Patients were randomly assigned to receive intravenous (i.v.) iron saccharate alone (control group), i.v. iron saccharate and subcutaneous rHuEPO 40,000 units once per week (group A) and i.v. iron saccharate and subcutaneous rHuEPO 40,000 units three times per week (group B). rHuEPO was given for a minimum of 2 weeks or until ICU discharge or death. The maximum duration of therapy was 3 weeks.

**Results** The cumulative number of RBC units transfused, the average RBC units transfused per patient and per transfused patient, the average volume of RBC transfused per day and the percent of transfused patients were significantly higher in the control group than those in groups A and B. No significant difference was observed between group A and group B. The mean increase in hematocrit (ΔHct) and Hb (ΔHb) from baseline to final measurement were significantly higher in group B than those in control group. ΔHct was significantly higher in group B than that in group A. ΔHct in group A was significantly higher than that in controls, whereas ΔHb did not differ significantly between the control group and group A.

**Conclusion** Administration of rHuEPO in critically ill patients significantly reduced the need for RBC transfusions. The magnitude of the reduction did not differ between the low and high doses of rHuEPO, whereas there was a dose response of Hct and Hb to rHuEPO in these patients.

## P337

### A randomised, placebo-controlled, double-blind study to investigate the efficacy and safety of rFVIIa as adjunctive therapy for control of bleeding in patients with severe blunt trauma: a re-analysis following the exclusion of early (< 48 hours) deaths

**R Rossaint[1], B Riou[2], K Boffard[3], Y Kluger[4], S Rizoli[5], B Warren[6], P Iau[7]**
*[1]University Hospital, Aachen, Germany; [2]Hôpital Pitié Salpêtrière, Paris, France; [3]Johannesbourg Hospital, Johannesbourg, South Africa; [4]Ichilov Hospital, Tel Aviv, Israel; [5]University of Toronto, Canada; [6]Tygerberg Hospital, Tygerberg, South Africa; [7]National University Hospital, Singapore*
*Critical Care* 2005, **9(Suppl 1):**P337 (DOI 10.1186/cc3400)

**Methods** Severely bleeding patients with blunt trauma were randomised to rFVIIa (200 + 100 + 100 μg/kg) or placebo as an adjunct to conventional treatment. Patients who had incurred both blunt and penetrating trauma were included in this study. First trial product injection followed the eighth RBC unit, with additional injections 1 hour and 3 hours later. The new efficacy analyses were performed on the patients surviving 48 hours or more after first administration of the trial product.
**Results** Of 153 blunt trauma patients randomised, 117 were eligible for the primary efficacy analysis (10 patients were excluded because they did not receive the trial product due to death or arrest of bleeding before transfusion of the eighth unit of RBC, and 26 patients were excluded due to death within the 48-hour period). Total RBC transfusion was significantly reduced with rFVIIa relative to placebo (estimated reduction of 2.6 total RBC units; 90% confidence interval: [0.7; 4.6]; $P = 0.02$) (results previously presented). The need for massive transfusion (> 20 RBC units, inclusive of the eight predose units administered pre trial product) was significantly reduced: 8/56 patients (14%) with rFVIIa versus 20/61 patients (33%) with placebo ($P = 0.03$), along with significant reductions in 48-hour requirements for FFP and platelets. The improved haemostasis was accompanied by a significant decrease in ARDS (3/56 [5%] of rFVIIa-treated vs 11/61 [18%] of placebo-treated patients [$P = 0.047$]) as well as a significant decrease in the risk of developing organ failure (either MOF or ARDS: 5/56 [9%] of rFVIIa-treated vs 15/61 [25%] of placebo-treated patients [$P = 0.047$]).
**Conclusions** Recombinant FVIIa improved clinical outcome (risk of developing single or multiple organ failure, especially ARDS) in severely bleeding blunt trauma patients. No safety issues were identified.

## P338

### The use of activated recombinant coagulation factor VII in patients undergoing major reconstruction surgery for traumatic fracture pelvis or pelvis and acetabulum: a double-blind, randomised, placebo-controlled trial

**R Raobaikady[1], J Redman[2], J Ball[3], G Maloney[4], R Grounds[1]**
*[1]St George's Hospital, London, UK; [2]York Hospital, York, UK; [3]Liverpool Hospital, New South Wales, Australia; [4]Mayo General Hospital, Co Mayo, Ireland*
*Critical Care* 2005, **9(Suppl 1):**P338 (DOI 10.1186/cc3401)

**Introduction** Activated recombinant coagulation factor VII (rFVIIa) effectively prevents and controls bleeding in patients with coagulopathy. Data show that rFVIIa may reduce blood loss and eliminate the need for transfusion in patients with normal haemostasis undergoing major surgery. We assessed the efficacy of rFVIIa in patients with normal haemostasis undergoing repair surgery of major traumatic fracture of the pelvis or the pelvis and acetabulum, who were expected to have a large volume of blood loss.
**Methods** We performed a double-blind, randomised, placebo-controlled trial involving 48 patients undergoing major pelvic-acetabular surgery. Patients were randomised to receive an intravenous bolus injection of 90 μg/kg rFVIIa or placebo as add-on therapy at the time of the first skin incision. All patients also received intraoperative salvaged red blood cells (RBC).
**Results** There was no significant difference in the total volume of perioperative blood loss, the primary outcome variable, between the rFVIIa and placebo groups (Table 1). In addition, there were no differences between the two groups in the total volume of blood components including salvaged RBC transfused, number of patients requiring allogeneic blood components, total volume of fluids infused, total operating time, time taken after entry to the intensive care unit to reach normal body temperature and acid–base status, and time spent in hospital. No adverse events, in particular thromboembolic events, were reported in either group.

**Table 1**

**Trial results**

| | rFVIIa ($n = 24$) | Placebo ($n = 24$) | *P* value |
|---|---|---|---|
| Total perioperative* blood loss (ml) | 2070 (431–6774) | 1535 (714–7057) | 0.79 |
| Intraoperative (ml) | 1598 (331–6574) | 1188 (514–6657) | 0.57 |
| Postoperative (ml) | 240 (0–1210) | 370 (80–650) | 0.022 |
| Total perioperative blood transfusion requirement (ml) | 289 (42–2365) | 706 (53–7138) | 0.33 |
| Salvaged RBC (ml) | 194 (0–935) | 171 (47–676) | 0.90 |
| Allogeneic RBC (units) | 0 (0–4) | 2 (0–16) | 0.34 |
| Number of patients transfused with allogeneic blood components | 11 (46%) | 16 (67%) | 0.24 |

Data presented as median (range) when applicable. *Perioperative period was defined as the intraoperative period combined with the 48 hours after the first dose of rFVIIa or placebo.

**Conclusions** In patients with normal haemostasis undergoing repair surgery of traumatic pelvic-acetabular fracture, the prophylactic use of rFVIIa does not decrease the volume of perioperative blood loss. Nevertheless, the use of rFVIIa appears to be safe in this patient population.

## P339

Abstract withdrawn

## P340

### Anti-Xa activity after subcutaneous administration of dalteparin in intensive care unit patients with and without subcutaneous oedema

**M Rommers[1], N van der Lely[2], T Egberts[1,3], P van den Bemt[1,3]**
*[1]Hospital Pharmacy Midden-Brabant, TweeSteden Hospital and St Elisabeth Hospital Tilburg, The Netherlands; [2]Intensive Care, St Elisabeth Hospital, Tilburg, The Netherlands; [3]Department of Pharmaco-epidemiology and Pharmacotherapy, Institute of Pharmaceutical Sciences, University of Utrecht, The Netherlands*
*Critical Care* 2005, **9(Suppl 1):**P340 (DOI 10.1186/cc3403)

**Introduction** Subcutaneous administration of low molecular weight heparins (LMWHs) is efficient in the prevention of venous

thromboembolism (VTE), which is a frequent complication in critically ill patients. ICU patients often suffer from subcutaneous oedema, due to the pathophysiology and large volumes of fluid they require. Subcutaneous oedema may impair the absorption of dalteparin, a LMWH, which is given by subcutaneous administration for VTE. To investigate whether indeed the absorption of dalteparin is impaired because of subcutaneous oedema, we compared the anti-Xa activity after subcutaneous injection of dalteparin in ICU patients with subcutaneous oedema with ICU patients without subcutaneous oedema.

**Methods** The study design is a non-randomised open parallel group follow-up study. The study was conducted at the ICUs (mixed medical–surgical) of two teaching hospitals in The Netherlands, from January 2003 until November 2004. The inclusion criteria were ICU patients with age >18 years, subcutaneous administration of dalteparin 2500 IU once daily for VTE prophylaxis. The exclusion criteria were use of vitamin K antagonists, use of therapeutic doses of LMWHs or UFH, severe liver failure, renal insufficiency, signs of disseminated intravascular coagulation, use of vasopressors and/or inotropics. Anti-Xa activities were determined at 0, 3, 4, 6, 8, 12 and 24 hours after subcutaneous administration of dalteparin. Both the Cmax and AUC(0–24 hours) values of anti-Xa activity were compared. Comparison of continuous variables was done by Student's *t* test. The anti-Xa activity (Cmax and AUC(0–24 hours)) was compared by the non-parametric Mann–Whitney test (mean ± standard error of the mean). A *P* value of 0.05 is taken as the cut-off for statistical significance.

**Results** Six ICU patients with and six ICU patients without subcutaneous oedema were studied. The characteristics of the index group were: age 57 years, male/female ratio 5/1, body mass index at admission 22.7 kg/m$^2$. The characteristics of the reference group were: age 48 years, male/female ratio 5/1, body mass index at admission 23.9 kg/m$^2$. In the index group creatinine clearance was lower compared with the reference group (81 vs 127 ml/min, $P = 0.57$). Both mean creatinine clearances were within the normal range. Sequential organ failure assessment score did not differ between the index and reference groups (4 vs 5). Mean arterial pressure was comparable between the index and reference group (87 vs 90 mmHg) and within the normal range. Mean plasma concentrations of factor anti-Xa activity were comparable in both groups. The mean Cmax value was not different between ICU patients with and without subcutaneous oedema (0.15 ± 0.02 vs 0.13 ± 0.03 IU/ml, $P = 0.30$). In the ICU patients with subcutaneous oedema the mean AUC(0–24 hours) value was higher (1.41 ± 0.34 vs 0.92 ± 0.11 hours IU/ml, $P = 0.23$).

**Conclusions** There is no difference in anti-Xa activity after subcutaneous administration of 2500 IU dalteparin between ICU patients with and without subcutaneous oedema. When compared with values in healthy volunteers, critically ill patients seem to have lower anti-Xa activity levels. This is found in recent studies as well. More research is necessary to identify the proper dose and route of LMWHs for VTE prophylaxis in ICU patients.

### P341

### *In vitro* effect of an antithrombin in platelet activation by HIT antibodies

**P Eichler, N Lubenow, R Raschke, A Greinacher**
*Ernst-Moritz-Arndt-University, Greifswald, Germany*
*Critical Care* 2005, **9(Suppl 1):**P341 (DOI 10.1186/cc3404)

**Purpose** Acute HIT usually precludes treatment with heparin. Clotting factor concentrates that contain heparin have also been regarded as contraindicated in these patients. Occurrence of HIT is currently shifting towards severely ill patients. These patients often require antithrombin (AT) substitution (e.g. for increased consumption in DIC). AT may contain heparin from the manufacturing process. In this study we assessed by means of an immunological assay whether heparin contaminations in AT can trigger platelet activation by HIT antibodies. As only 30% of heparins contain the AT binding pentasaccharide, determination of FXa activity is not sufficient to detect immunological relevant heparin concentrations.

**Methods** After thawing and heat inactivation, HIT sera were tested in the $^{14}$C-serotonin release assay ($^{14}$C-SRA) in the presence of heparin or two AT batches at different concentrations (undiluted, 1/2, 1/4, 1/8, 1/16, 1/32, 1/64, 1/128; one batch unspiked, one batch spiked with 1 IU heparin/ml) (Atenativ®; Octapharma AB, Stockholm, Sweden). A reaction in the presence of AT was considered positive if the $^{14}$C-SRA was > 20% with at least two of four platelet donors.

**Results** Sera of 10 patients with documented clinical HIT were investigated. Using the unspiked AT batch only one of 10 HIT sera showed weak platelet activation in the $^{14}$C-SRA at a dilution of AT of 1:16 but not at less diluted AT. This indicates a false positive reaction rather than a real HIT-dependent platelet activation. With the spiked AT batch the sensitivity of the assay was determined to detect at least a concentration of 0.06 IU heparin/ml AT.

**Conclusion** The antithrombin concentrate we tested does not contain ≥ 0.06 IU/ml heparin. Considering a worst-case scenario, treating a HIT patient with 1000 IU Atenativ® might theoretically result in a final heparin plasma concentration of maximally $0.2 \times 10^{-3}$ IU/ml whole blood. It is unlikely that this amount of heparin will cause adverse effects in a HIT patient.

### P342

### The effect of fibrinogen and prothrombin complex concentrate on dilutional coagulopathy in a porcine model of uncontrolled hemorrhagic shock

**D Fries[1], T Haas[1], W Streif[2], K Ebert[1], A Klingler[3], P Innerhofer[1]**
*[1]Department for Anesthesiology and Critical Care Medicine, Medical University Innsbruck, Austria; [2]Department for Pediatrics, Medical University Innsbruck, Austria; [3]Department for Theoretical Surgery, Medical University Innsbruck, Austria*
*Critical Care* 2005, **9(Suppl 1):**P342 (DOI 10.1186/cc3405)

**Purpose** Dilutional coagulopathy is a common complication in severely injured patients and a consequence of blood loss, administration of synthetic colloids and red blood cell concentrates to compensate huge blood losses. This study was conducted to assess whether substituting the combination of fibrinogen and prothrombin complex concentrate (PCC) enables the reversal of dilutional coagulopathy, and whether this treatment leads to a reduction in further blood loss and mortality.

**Methods** Anesthetized pigs ($n = 20$) were instrumented for blood sampling and hemodynamic monitoring. About 66% of the calculated blood volume was withdrawn and replaced with hydroxyethylstarch (130 HES 0.4). Then, pigs were randomized to receive either 200 mg/kg fibrinogen and 35 IE/kg PCC ($n = 10$) or placebo ($n = 10$). Thereafter, a standard liver laceration was performed to induce uncontrolled hemorrhage. Modified thrombelastography was used to assess the dynamics and quality of clot formation.

**Results** After hemodilution both groups showed statistically significant increased clotting times (CT), clot formation times (CFT), and decreased maximum clot firmnesses (MCF). After fibrinogen and PCC administration, CT and CFT decreased whereas MCF increased statistically significantly. Median blood loss after liver injury was significantly smaller in the animals treated

with clotting factor concentrates versus the placebo group: 240.0 ml (50.0–830.0) vs 1.800 ml (1.500–2.500) ($P < 0.0001$). All animals, treated with fibrinogen and PCC survived, whereas 80% of the placebo group died after liver laceration ($P < 0.0001$).
**Conclusion** During hemodilution, substitution of fibrinogen and PCC leads to an enhancement in coagulation and final clot strength. This reversal of dilutional coagulopathy may reduce blood loss and mortality when large amounts of colloids are needed to maintain normovolemia during huge blood losses.

### P343

### Consensus protocol for the emergency reversal of coumarin-induced anticoagulation

**G Dolan[1], D Bevan[2], P Giangrande[3], K Hampton[4], C Hay[5], C Ludlam[6], B McVerry[7], K Pasi[8], M Winter[9]**
*[1]University Hospital, Nottingham, UK; [2]St George's Hospital, London, UK; [3]Chuchill Hospital, Oxford, UK; [4]Royal Hallamshire Hospital, Sheffield, UK; [5]Manchester Royal Infirmary, Manchester, UK; [6]Edinburgh Royal Infirmary, Edinburgh, UK; [7]St James Hospital, Leeds, UK; [8]Royal London Hospital, London, UK; [9]Kent & Canterbury Hospital, Canterbury, UK*
*Critical Care* 2005, **9(Suppl 1):**P343 (DOI 10.1186/cc3406)

The management of haemorrhage or risk of haemorrhage in anticoagulated patients increasingly involves those providing services for haemophilia. This is particularly so in the use of prothrombin complex concentrates where experience of the use of these products exists almost entirely within haemophilia centres. As the majority of bleeding anticoagulated patients present to hospitals that do not have haemophila centres, and where there is little experience in the use of PCCs, there is clearly a need for practical guidelines to guide use of these products. Clinicians must be made aware of the potential benefits and risks of using concentrated coagulation factors prepared from large plasma pools.
A key aspects of the safe use of PCCs is the careful selection of the clinical indications for their use. Only those patients with or at risk from life-threatening haemorrhage should be treated. And where a licensed product is available, this should be used in preference to those that are not.
Data are lacking on the comparative efficacy of products containing factors II, VII, IX (FIX) and X against those lacking factor VII. There is evidence to show that factor VII levels may be extremely low in patients with high INRs, suggesting that overanticoagulated patients may benefit more from PCCs containing all four vitamin K-dependent factors.
The optimal dose of PCC required to reverse anticoagulation is not fully established but does depend on the degree of the coagulation defect. The experience of this group suggests that doses between 25 IU FIX/kg and 50 IU FIX/kg are effective.
We present a practical protocol for the use of PCC in reversal of coumarin-induced anticoagulation.

### P344

### Warfarin overactivity

**L Yamanel, B Comert, V Inal, I Naharci**
*GATA, Ankara, Turkey*
*Critical Care* 2005, **9(Suppl 1):**P344 (DOI 10.1186/cc3407)

**Background** The number of patients anticoagulated with warfarin has rapidly increased over the past decade. Although warfarin is a highly effective anticoagulant agent, bleeding diathesis is not an uncommon complication of this treatment. Approximately 1% of these patients annually experience serious bleeding, and 0.5% dies. Warfarin is a special drug, which interacts with many drugs and food. These interactions of the drug make its therapeutic monitoring very problematic.
**Method** The present study was performed at the Medical Intensive Care Unit (MICU) of Gulhane School of Medicine between 1 January and 31 December, and 22 patients with hemorrhagic complication-related warfarin usage were enrolled into the study. All of the 22 patients had International Normalized Ratio (INR) > 4.
**Results** The average age was 69.7 years, and 66 (73%) of these patients were women. Warfarin was most frequently prescribed for chronic atrial fibrillation (55%). All of the patients with hemorrhage due to warfarin toxicity had received concomitant drugs, which may be responsible for the overactivity of warfarin. The INRs of 13 patients (59%) were ranged between 4.0 and 10.0, and for the remaining patients were above 10.0. Epistaxis, hematuria, and hemarthrosis (minor bleeding) has occurred in all patients with INRs between 4.0 and 10.0, and these patients were given according to our MICU protocols parenteral vitamin K replacements. Patients were discharged from the MICU when hemostasis was established, and vitamin K administration continued by appropriate on an outpatient basis. Patients with INR of 10.0 and above ($n = 9$) were treated with fresh frozen plasma transfusions (2–5 units). Massive upper gastrointestinal bleeding was observed in five (55%) of these patients, which were in the seventh–eighth decades. One of them has died besides fresh frozen plasma and erythrocyte transfusions and endoscopic procedures applied for all. In one patient with INR of 13.4, bleeding from ears was interestingly observed. The average length of ICU stay for all patients was 3.2 days.
**Conclusion** Although the patients on warfarin treatment were strictly monitored, hemorrhage is not an uncommon problem and these patients need ICU support. Many patients receiving warfarin therapy are treated with concomitant drugs that may interact with the warfarin. The high percentage of patients taking drugs that may increase the INR or bleeding risk is a reminder that bleeding events are a probable adverse outcome of combining drugs that interact with warfarin.

### P345

### Role of thromboelastography in septic patients treated with coagulation inhibitor

**A Giarratano, S Raineri, D Canzio**
*Azienda Ospedaliera Universitaria Policlinico, Palermo, Italy*
*Critical Care* 2005, **9(Suppl 1):**P345 (DOI 10.1186/cc3408)

**Introduction** Substitutive treatment with coagulation natural inhibitors could be associated with severe bleedings in surgical patients. We evaluate the role of thromboelastography (TEG) in monitoring of septic patients during treatment with AT III and aPC.
**Methods** We enrolled all the patients admitted in ICU for more 48 hours with surgical severe sepsis associated with severe deficiency of coagulation natural inhibitors. Two groups were created. Group A treated with activated PC 24 μg/kg for 96 hours and Group B with, in addition, AT III administered by the target [(140 – AT III dosed) × BW (kg)]. TEG was registered before, at the beginning, during the treatment every 12 hours and 24 hours after the end of administration. We also registered the SOFA score until discharge.
**Results** The clinical data and results are presented in Tables 1 and 2.
**Conclusions** TEG allows, at the bedside, the dynamic monitoring of coagulation systems. APC has an anticoagulant and profibrinolitic role without haemorrhagic effects and this is registered by TEG. It is interesting to notice that the use of AT III and aPC in the

**Table 1 (abstract P345)**

| | | Pretreatment | | | | During treatment | | |
|---|---|---|---|---|---|---|---|---|
| | *n* | SOFA | *r* | MA | Ly 30 | r | MA | Ly 30 |
| aPC | 6 | 9 ± 2 | 2 ± 1 | 76 ± 11 | 2 ± 1 | 18 ± 6 | 56 ± 22 | 9 ± 5 |
| AT + aPC | 4 | 9 ± 3 | 3 ± 2 | 77 ± 9 | 3 ± 1 | 19 ± 6 | 57 ± 17 | 11 ± 5 |

**Table 2 (abstract P345)**

| | | 24-hour after treatment | | | |
|---|---|---|---|---|---|
| | *n* | SOFA | *r* | MA | Ly 30 |
| aPC | 6 | 6 ± 3 | 8 ± 3 | 71 ± 22 | 6 ± 3 |
| AT + aPC | 4 | 7 ± 3 | 7 ± 4 | 75 ± 15 | 7 ± 2 |

septic patients has no haemorrhagic effects and this is also confirmed by SOFA and by our preliminary data about 28-day mortality. We believe that the TEG could solve a lot of problems related to the correct timing of sepsis and to inhibitor treatment.

## P346

## Thromboelastography during treatment with activated protein C

**E Panascia, G Castiglione, P Calabrese, S Saglimbene, B Panascia**
*Azienda Ospedali Vittorio Emanuele, Catania, Italy*
*Critical Care* 2005, **9(Suppl 1):**P346 (DOI 10.1186/cc3409)

**Introduction** Activated protein C (rhAPC) infusion increases fibrinolysis, which is very difficult to evaluate with standard tests. We used TEG to monitor the coagulation in our patients during the infusion of rhAPC.

**Materials and methods** Six patients with severe sepsis were treated with rhAPC (24 µg/kg/hour for 96 hours). TEG (ETEG 3000; Hemoscope Corp., Skokie IL, USA) was carried out on native blood before (T0), at 24 hours (T1), 48 hours (T2), 72 hours (T3), 96 hours (T4) during and 24 hours after the end (T5) of rhAPC treatment. Analysis of differences between data was carried out with the Student *t* test for paired data (differences statistically significant for $P < 0.05$).

**Results** Data are expressed as the mean and standard deviation. Results obtained are shown in Table 1 and Figs 1 and 2. * indicates the statistically significant results.

**Discussion** TEG is a reliable tool for monitoring fibrinolysis during rhAPC. Fibrinolyisis is more evident during the first 48 hours of infusion, probably because of a new equilibrium in the coagulation system reached after that period.

**Figure 1 (abstract P346)**

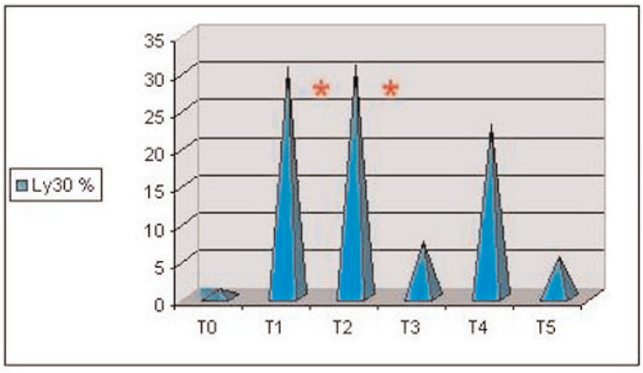



**Figure 2 (abstract P346)**

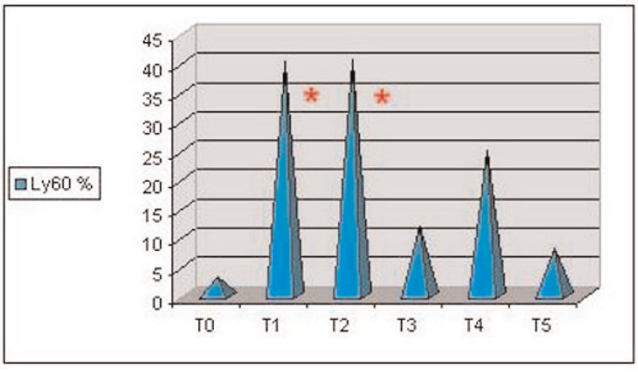



**Table 1 (abstract P346)**

| | T0 | T1 | T2 | T3 | T4 | T5 |
|---|---|---|---|---|---|---|
| R min | 29.4 (16.6) | 67.4 (70.6) | 54.1 (33.6) | 47.6 (15.2) | 52.9 (34.3) | 38.5 (43.6) |
| K min | 11.7 (5.8) | 21.4 (29.6) | 14 (10.2) | 18.5 (18.2) | 19.4 (19.4) | 23.1 (37.6) |
| MA mm | 64.9 (12.4) | 60.7 (20.9) | 65.2 (19.6) | 66.3 (22.6) | 64.8 (18.3) | 58.7 (21.5) |
| ANG ° | 43.1 (13.4) | 41.8 (22.6) | 40.8 (15.7) | 40.7 (23.2) | 35.8 (20.6) | 45.7 (25.7) |
| Ly 30% | 1 (1.1) | 30.5* (22.9) | 30.8* (26.4) | 7.4 (10) | 22.8 (25.8) | 5.4 (5.6) |
| Ly 60% | 3.1 (3.3) | 40* (22.6) | 40.3* (26.6) | 11.8 (14.6) | 24.8 (32.1) | 8.1 (4.7) |

## P347

### Coagulation changes during pregnancy and delivery: adjustment of reference ranges for thrombelastography and for some laboratory tests is necessary

**F Polak, H Bedrichova, P Kriz, L Bohacenkova, M Lips, A Parizek, J Kvasnicka**
*General University Hospital, Prague, Czech Republic*
*Critical Care* 2005, **9(Suppl 1):**P347 (DOI 10.1186/cc3410)

**Hypothesis** The coagulation status in pregnant women is different from the general population in so far that we must adjust the reference range of coagulation tests for these women.
**Objective** To compare the coagulation parameters in pregnant and parturient women to normal ranges used for the general population. If there is a significant difference between these groups, set new ranges for thrombelastography and/or coagulation laboratory tests.
**Participants** Sixty healthy pregnant women (group HPW) were divided into two subgroups: 30 in the third trimester (subgroup TT) and 30 in the first period of delivery (subgroup FP).
**Design and methods** A prospective nonintervention study. In all women we performed thrombelastography and coagulation laboratory tests. Thrombelastography was performed from native blood after activation by 1% cellite. Blood samples were obtained from the peripheral vein, before any medical intervention.
**Results** The mean of all thrombelastographic parameters in the HPW group was in the normal range set for the general population, but mostly very close to a 'procoagulation' limit (mean time *r* 4.7 ± 1.7; time *k* 1.5 ± 0.5; alpha angle 69.6 ± 5.5; maximal amplitude 71.3 ± 4.5; coagulation index 2.7 ± 1.8); there was no statistically significant difference between subgroups TT and FP. In laboratory tests, the majority of parameters was also close to the 'procoagulation' limit of the normal range and, in addition, three of the parameters were outside the normal range (mean fibrinogen 5.2 ± 0.6; D-dimers 349.9 ± 138.6; protein S 42.4 ± 13.7). After the statistical analysis we adjusted the reference ranges for pregnant women. Some of our recommendations for thrombelastography are presented in Table 1.

**Table 1**

| | Time *r* | Time *k* | Alpha angle | Maximal amplitude | Coagulation index |
|---|---|---|---|---|---|
| Normal population | 4–8 | 1–4 | 47–74 | 55–73 | −3 to +3 |
| Pregnant women | 2–8 | 1–3 | 60–77 | 64–76 | 0–5 |

**Conclusions** For assessment of coagulation status by thrombelastography and for some laboratory tests in pregnant and parturient women, it is necessary to set new reference ranges that are different from those for the normal population.
**Acknowledgements** Supported by grant IGA MZ No. NR/8157-3 and VZ 64165.

## P348

### The histopathologic effects on organs of desmopressin administered to rats in different doses

**G Kutuk, L Dösemeci, M Cingi, T Gelen, H Gülmez, S Atalay, E Nizamoglu, A Ramazanoglu**
*University of Akdeniz, Antalya, Turkey*
*Critical Care* 2005, **9(Suppl 1):**P348 (DOI 10.1186/cc3411)

**Objectives** Desmopressin is a synthetic analogue of vasopressin. It leads to the release of vWF, FVIII-C, t-PA, P-selectin from endothelium, microthrombus and thromboembolism. In this study, the histopathologic effects of intravenous (i.v.) desmopressin given both in normal and high doses on organs of rats were studied.
**Materials and methods** This study was performed in 5-month-old female rats of WISTAR type with the consent of the Ethics Committee of Experimental Animals. Three groups each consisting of 10 rats were formed. Following anesthesia and catheterization, the first group did not receive desmopressin (control). Desmopressin was administered slowly by i.v. route to group 2 and group 3 at 1.5 μg/kg and 4.5 μg/kg bolus doses, respectively. A 25 ml/kg/hour dose of 0.9% NaCl infusion was administered into each group. After 4 hours, laparatomy and thoracotomy were performed and the kidneys, pancreas, liver and heart were removed with their vessels using normal procedures (without damaging the stricture of the organs). These organs were examined histopathologically. Appearances of specimens were graded and evaluated statistically using the Mann–Whitney U test.
**Results** Normal findings were obtained in the histopathologic examinations of the liver, kidneys and heart. But mild inflammation, vacuolization, necrosis, microthrombus, and damage of endothelium were determined in the pancreas examinations of all groups. A significant difference was found in terms of the damage of the endothelium between groups in the pancreas (group 1 < group 3 and group 2 < group 3). In addition, a significant difference was found between group 1 and group 2 (group 1 < group 2) in vacuolization. A significant difference was not found in the appearances of microthrombus, inflammation and necrosis among groups.
**Conclusions** There is concern that desmopressin, used in the treatment of diabetes insipidus, may cause formation of thrombus, especially in the microvascular bed, and so this may result in disorders in the perfusion of target organs. But in our study, even though desmopressin was administered in high doses, it did not cause thromboembolic damages in several organs and capillary endothelium, and for this reason it can be used safely.

## P349

### Continuous hemodiafiltration for hypercytokinemia in tumor lysis syndrome

**M Nakamura, H Hirasawa, S Oda, H Shiga, K Matsuda, E Watanabe**
*Department of Emergency & Critical Care Medicine, Graduate School of Medicine, Chiba University, Chiba, Japan*
*Critical Care* 2005, **9(Suppl 1):**P349 (DOI 10.1186/cc3412)

Tumor lysis syndrome (TLS) is a critical condition being presented with hyperuricemia, electrolyte disturbance and acute renal failure, and it is thought to be caused by massive release of cellular breakdown products due to substantial destruction of tumor cells. Some TLS patients develop multiple organ failure. Blood purification, such as hemodialysis is often performed on patients with TLS as a renal replacement therapy. We noticed that some TLS patients also had hypercytokinemia and speculated that such hypercytokinemia might be associated with the pathophysiology of TLS. On the other hand, we reported that continuous hemodiafiltration using a polymethyl methacryrate membrane hemofilter (PMMA-CHDF) can eliminate cytokines from the blood stream of patients. We therefore applied PMMA-CHDF on four patients with TLS with the expectation that PMMA-CHDF also can be an effective treatment against hypercytokinemia in TLS patients. All patients had hematological malignancy and received induction antitumor chemotherapy. During the chemotherapy, they developed hyperuricemia, hyperpotassemia and acute renal failure, and were diagnosed to have TLS. Two of them developed multiple organ

failure. In one patient the failing organs were the lung and kidney, and in the other patient the failing organs were the heart, lung and kidney. In all TLS patients, blood levels of tumor necrosis factor alpha, IL-6 and IL-10 before the initiation of PMMA-CHDF were 102 ± 85 pg/ml, 1097 ± 546 pg/ml and 98 ± 83 pg/ml, respectively (mean ± standard deviation). After 3 days of CHDF treatment, blood levels of those cytokines were 37 ± 55 pg/ml, 326 ± 511 pg/ml, and 9 ± 8 pg/ml, respectively. All cytokine levels were thus significantly decreased with 3 days of PMMA-CHDF treatment ($P < 0.05$, $P < 0.05$, $P < 0.05$, paired *t* test). After the PMMA-CHDF treatment, their clinical conditions were improved, and all patients survived. In one of these patients, the blood levels of each cytokine before and after the PMMA membrane homofilter were measured and the clearance of these cytokines was calculated. The clearance of each cytokine is as follows; tumor necrosis factor alpha 13.9 ± 6.4 ml/min, IL-6 4.9 ± 2.4 ml/min, IL-8 21.6 ± 3.9 ml/min and IL-10 11.1 ± 6.4 ml/min,. From those results, we conclude that TLS could be caused by hypercytokinemia probably due to massive tumor cellular breakdown by chemotherapy and that PMMA-CHDF is an effective treatment for TLS patients not only as renal replacement therapy, but also as a cytokine modulator.

## P350

### Anticoagulation during continuous renal replacement therapy with lepirudin in patients with heparin-induced thrombocytopenia

**T Schroeder, C Karcher, G Engelmann, W Krueger, K Unertl**
*University of Tuebingen, Germany*
*Critical Care* 2005, **9(Suppl 1):**P350 (DOI 10.1186/cc3413)

**Introduction** Heparin-induced thrombocytopenia type II is a serious complication during heparin therapy. Treatment with lepirudin is an alternative when anticoagulation is indispensable. However, lepirudin accumulates in patients with acute renal failure treated with renal replacement therapy. This might lead to an increase in bleeding complications, longer ICU length of stay, and more therapeutic interventions. We conducted a retrospective study of all patients after cardiothoracic surgery that developed acute renal failure, treated by continuous renal replacement therapy, during a 17-month study period. We grouped the patients according to anticoagulation with heparin or lepirudin, respectively, and analyzed the groups for differences in length of ICU stay, bleeding complications, scores (APACHE II, SAPS, TISS), and mortality.
**Methods** One hundred and thirty-seven (7.2%) of a total of 1888 patients were treated with renal replacement therapy. Of those, eight patients received lepirudin, due to confirmed heparin-induced thrombocytopenia, and the remaining 129 patients were treated with heparin. Continuous heparin and lepirudin treatment was adjusted to an activated partial thromboplastin time of 1.5 times baseline values. Age, sex, type of surgery, re-operation, transfusion requirements, APACHE II score, SAPS score, TISS76 score, length of ICU stay, and ICU mortality were recorded. Statistical analysis was performed by chi-square test, likelihood ratio test, and Wilcoxon–Kruskal–Wallis test, where appropriate. Data are expressed as mean ± standard deviation, or median with 25th–75th percentiles.
**Results** Patients that were anticoagulated with lepirudin remained significantly longer in the ICU (18 [13.5–53.25] vs 7 [3–16.5] days; $P = 0.013$). Lepirudin-treated patients were transfused significantly more frequently with packed red blood cells, and pooled thrombocytes (packed red blood cells 7 [3–15] vs 17 [8.25–27] units; $P = 0.037$; pooled thrombocytes 3.5 [1–8.5] vs 1 [0–2] units; $P = 0.025$). Additionally, these patients had significantly higher TISS scores (53 [44.75–62.25] vs 50 [44–53.5] adjusted for days; $P = 0.046$). Age, sex, number of re-operations, APACHE II score, SAPS score, type of surgery, and mortality did not differ significantly between the groups.
**Conclusion** Lepirudin treatment after cardiac surgery in patients that develop acute renal failure, treated with continuous renal replacement therapy, leads to longer ICU length of stay, higher transfusion requirements, and more therapeutic interventions, and thus higher costs.

## P351

### Renal replacement therapy for acute renal failure in the intensive care unit is associated with a worse prognosis than renal replacement therapy for end-stage renal failure

**M Ostermann, R Chang**
*St George's Hospital, London, UK*
*Critical Care* 2005, **9(Suppl 1):**P351 (DOI 10.1186/cc3414)

**Background** Renal failure in critically ill patients is perceived as a serious problem with high mortality.
**Objectives** To compare the outcome of ICU patients with renal failure requiring renal replacement therapy (RRT) with that of patients without renal failure (defined by a serum creatinine <120 µmol/l) and to determine whether there is a difference in outcome between ICU patients with acute renal failure (ARF) treated with RRT and ICU patients with pre-existing dialysis-dependent end-stage renal failure (ESRF).
**Methods** Retrospective analysis of the Riyadh ICU Program database of 41,972 patients admitted to 22 ICUs in the United Kingdom and Germany between 1989 and 1998.
**Results** Table 1 presents the characteristics and outcome of patients with and without renal failure. Table 2 outlines the association between the maximum number of other failed organ systems (as defined by criteria of Knaus and colleagues, excluding renal failure) and ICU mortality in ARF patients and patients with ESRF.
**Conclusions** The need for renal replacement therapy in the ICU was associated with an increased mortality. Patients who needed RRT for ARF had a longer stay in the ICU and a significantly higher mortality compared with patients who had RRT for pre-existing ESRF. This difference in outcome was most probably due to other factors, including number of associated failed organ systems.

**Table 1 (abstract P351)**

| | Total population | No renal failure | ARF and RRT | ESRF and RRT |
|---|---|---|---|---|
| Number of patients | 41,972 | 29,225 | 1787 | 797 |
| Mean age (95% CI) | 60.5 (60.3–60.6) | 59 (59–59.4) | 60 (60–61) | 55 (54–56) |
| Male sex (%) | 63.5 | 61.8 | 67.4 | 59.6 |
| Median APACHE II score (day 1) | 13 | 11 | 23 | 21 |
| Length of stay in ICU (days) | 2 | 1 | 10 | 2 |
| ICU mortality (%) | 13.7* | 6.2* | 54.6* | 20.8* |
| Hospital mortality (%) | 18.8* | 10.3* | 62.3* | 34.5* |
| Standardized mortality ratio (%) | 1.08 | 0.86 | 1.49 | 0.97 |

* $P < 0.0001$.

**Table 2 (abstract P351)**

| Maximum number of other failed organs | ARF and RRT: Proportion of patients (%) | ARF and RRT: ICU mortality (%) | ESRF and RRT: Proportion of patients (%) | ESRF and RRT: ICU mortality (%) | *P* value |
|---|---|---|---|---|---|
| 0 | 9.7 | 12.1 | 42 | 2.7 | < 0.0001 |
| 1 | 22.9 | 35.7 | 32.4 | 14.7 | < 0.0001 |
| 2 | 34.0 | 56.8 | 16.7 | 48.1 | NS |
| > 2 | 33.4 | 78.2 | 8.9 | 77.5 | NS |

## P352

### The effect on renal function in high pulmonary flow infants under hypoxic therapy

**A Asakura, A Miyaji, H Hayami, O Yamaguchi, H Oki, S Nagai, A Kokawa, K Akita, Y Oi**
*Yokohama City University Medical Center, Yokohama, Japan*
*Critical Care* 2005, **9(Suppl 1):**P352 (DOI 10.1186/cc3415)

**Objective** To evaluate the effect on renal function in high pulmonary flow infants under hypoxic therapy.
**Patients and methods** The patients were eight infants with heart failure due to high pulmonary flow who needed to use nitrogen before surgical correction. Nitrogen was administered through the oxygen inlet line of a Servo 300® ventilator and $FiO_2$ was kept in the range 0.13–0.18. Creatinine clearance (CCr), $CH_2O$, and FENa were measured daily until the operation.
**Results** CCr increased from 30 ± 1.7 ml/min to 42 ± 24 ml/min, while $PO_2$ decreased from 47.4 ± 8.42 mmHg ($FiO_2$ 0.21) to 40.0 ± 6.06 mmHg ($FiO_2$ 0.16 ± 0.02).
**Conclusion** Hypoxic therapy for high pulmonary flow infants improved creatinine clearance as well as pulmonary flow.

## P353

### Prophylaxis of contrast-induced nephropathy in patients with impaired renal function: double-blind comparison of acetylcysteine, theophylline, acetylcysteine + theophylline and placebo

**W Huber[1], C Schilling[1], A Wacker[2], M Hennig[3], L Greiner[1], T Rutz[2], A Umgelter[2], F Eckel[1], B Vogelsang[1], A Schoemig[2], U Heemann[1], R Schmid[1]**
*[1]Second Medical Department, Klinikum Rechts der Isar, Munich, Germany; [2]1st Medical Department, Munich, Germany; [3]Institute for Medical Statistics and Epidemiology, Munich, Germany*
*Critical Care* 2005, **9(Suppl 1):**P353 (DOI 10.1186/cc3416)

**Background** Contrast-induced nephropathy (CIN) is frequently found in ICU patients. Several recent studies have shown a prophylactic effect of acetylcysteine (A) and theophylline (T). The results are contradictory, however, and only one study has so far compared the effects of both agents [1]. Nevertheless, this study did not include a placebo group and was not restricted to patients with impaired renal function.
**Aim** To compare the effects of A, T, a combination of A and T (A + T) and placebo (P) in patients with impaired renal function.
**Materials and methods** Two hundred and fifty-four patients with serum creatinine ≥ 1.3 mg/dl receiving ≥ 100 ml contrast-medium (CM) were randomised to receive A (600 mg, p.o., b.i.d.; start 24 hours before CM), T (200 mg, i.v., 30 min before CM), A + T, or P. *Primary endpoint* The incidence of CIN (increase of serum creatinine ≥ 0.5 mg/dl within 48 hours). *Secondary endpoint* Time course of serum-creatinine. *Statistics* Chi-square-test and Wilcoxon-test, SAS software version 6.12.
**Results** Patients of groups A, T, A + T and P were comparable with regard to baseline creatinine (1.49 ± 0.43 vs 1.53 ± 0.56 vs 1.57 ± 0.40 vs 1.69 ± 0.77 mg/dl; not significant [NS]), amount of CM (192.5 ± 104.3 vs 240.2 ± 149.9 vs 222.7 ± 141.9 vs 207.6 ± 113.6 ml; NS) and incidence of other risk factors (RF) such as diabetes and hypertension. The incidence of CIN was 4/62 (6.5%) in group A, 3/64 (4.7%) in group T, 7/66 (10.6%) in group A + T, and 10/62 (16.1%) in group P. Overall, the incidence was lower under prophylaxis (14/192; 7.3%) than under placebo (10/62, 16.1%; $P = 0.0386$). Patients of group T had a significantly lower incidence of CIN than patients under placebo ($P = 0.0348$), whereas neither group A nor group A + T had a lower incidence of CIN than group P.
Compared with baseline, serum creatinine levels significantly increased after 48 hours in group A (1.54 ± 0.39 vs 1.49 ± 0.43 mg/dl; $P = 0.00986$), group A + T (1.63 ± 0.41 vs 1.57 ± 0.40 mg/dl; $P = 0.0075$) and group P (1.80 ± 0.85 vs 1.69 ± 0.77 mg/dl; $P = 0.00619$). However, there was no significant increase in group T (1.56 ± 0.55 vs 1.53 ± 0.56 mg/dl; NS).
**Conclusions** In patients with impaired renal function theophylline significantly reduces the incidence of CIN, whereas acetylcysteine alone or in combination with theophylline was not effective.
**Reference**
1. *Intensive Care Med* 2002, **28(suppl 1):**S139.

## P354

### Insulin-like growth factor-1 during renal replacement therapy in patients with multiple organ failure

**I Yakovleva[1], V Timokhov[2], G Lialikova[1]**
*[1]Common Reanimatology, Moscow, Russia; [2]Russian Medical Academy of Postgraduate Edication, Moscow, Russia*
*Critical Care* 2005, **9(Suppl 1):**P354 (DOI 10.1186/cc3417)

**Introduction** Insulin-like growth factor-1 (IGF-1) protein (7650 Da) has a strong anabolic effect. Secretion of IGF-1 fails in a number of pathologies, and this deficit can increase during renal replacement therapy (RRT) procedures.
**Materials** Eleven patients (nine males/two females, mean age 49.5 ± 3.7 years) with multiple organ failure (MOF) were examined. APACHE II score was 27.8 ± 0.6. Eight patients had sepsis (72.7%). Ten patients underwent mechanical lung ventilation. Six patients received an inotropic support (54.5%). The mortality rate was 54.5%. Hemoprocessors 'Prisma' (Hospal, France) and 'Aquarius' (Edwards, Germany) were used for RRT. Retrospectively, two groups were selected: Group A ($n = 5$), treated by hemofiltration (HF), with mean duration of procedures 57.1 ± 6.4 hours, effluent volume 66.0 ± 7.1 l/day; and Group B, treated by hemodiafiltration (HDF), mean duration 49.1 ± 5.7 hours, effluent volume 103.2 ± 3.5 l/day. IGF-1 levels were measured using an ELISA assay (DRG, Germany).
**Results** During RRT procedures in Group A the plasma concentration of IGF-1 fluctuated on average from 42.6 to 46.8 ng/ml, in Group B it ranged from 18.1 to 39.8 ng/ml (in healthy men – 150–300 ng/ml). The concentration of IGF-1 in effluent in both groups varied from 14.2 to 25.9 ng/ml and had no statistically significant difference. Elimination of IGF-1 in Group A during HF was 1389.4–1678.9 μg/day and in Group B during HDF was 1741.3–2446.9 μg/day. Clearance IGF-1 was 21.6 ml/min during HF and 56.8 ml/min during HDF due to the large volumes of effluent during the procedures.

**Conclusion** A relative deficit in IGF-1 was found in patients with MOF that possibly could be increased by intensive RRT. The preliminary data show the necessity of early usage of this growth factor in patients with MOF.

## P355

## Clearance of Sotalol on continuous venovenous haemofiltration

**H Roberts, N Stallard**
*University Hospital of Wales, Cardiff, UK*
*Critical Care* 2005, **9(Suppl 1):**P355 (DOI 10.1186/cc3418)

**Introduction** Sotalol is a non-selective beta blocker with class III antiarrhythmic properties. It is not protein bound and is mostly excreted unchanged in the urine. Both peritoneal dialysis [1] and haemodialysis [2] have been successful in treating Sotalol-induced arrhythmias in the prescence of renal failure. Clearance of Sotalol by continuous venovenous haemofiltration (CVVH) is not described. We report a case of massive Sotalol overdose in which CVVH was successfully used.
**Patient** A 53-year-old lady presented following a deliberate overdose of Sotalol tablets. She was admitted to the ITU in multiple organ failure requiring mechanical ventilation, vasopressors and renal replacement therapy. CVVH was commenced 15 hours after the overdose using an exchange of 6000 ml/hour (approximately 70 ml/kg/hour) on a Baxter 'Aquarius' machine. High-flow CVVH was continued for 48 hours before reducing to 3000 ml/hour. CVVH was required for 21 days in total. The patient was discharged home without significant morbidity 2 months after admission.
**Methods** Paired plasma and filtrate samples were collected at intervals during the first 24 hours of CVVH. These were analysed for Sotalol concentration using a HPLC assay. Plasma clearance was estimated using the formula C = UV / P, where C = clearance (ml/min), U = filtrate concentration (mg/ml), V = filtrate volume (ml/min) and P = plasma concentration (mg/ml).
**Results** See Table 1. Mean clearance = 67.00 ± 6.64 ml/min.

**Table 1**

| Time | Plasma concentration | Filtrate concentration | Clearance |
|---|---|---|---|
| 15:30 | 0.0235 | 0.013 | 55.32 |
| 17:30 | 0.0156 | 0.0111 | 71.15 |
| 21:30 | 0.0177 | 0.0121 | 68.36 |
| 01:30 | 0.0142 | 0.0105 | 73.94 |
| 05:30 | 0.0114 | 0.0082 | 71.93 |
| 09:30 | 0.011 | 0.0074 | 67.27 |
| 13:30 | 0.01 | 0.0061 | 61.00 |

**Conclusion** Clearance of Sotalol by CVVH is significant and should be considered as an adjunct in cases of Sotalol toxicity and renal insufficiency. CVVH is likely to cause less cardiovascular instability than the previously described methods [1,2] of increasing drug clearance.
**Acknowledgement** The authors would like to thank Guy's and St Thomas' Medical Toxicology Unit for their assistance with the Sotalol assay.
**References**
1. Tang S, *et al.*: *Perit Dial Int* 1997, **17:**207-208.
2. Van Uum SH, *et al.*: *Nephrol Dial Transplant* 1997, **12:**331-333.

## P356

## Prevalence, incidence and risk factors for acute renal failure in the intensive care unit

**C Rabbat, E McDonald, L Griffith, F Clarke, D Cook**
*McMaster University, Hamilton, Canada*
*Critical Care* 2005, **9(Suppl 1):**P356 (DOI 10.1186/cc3419)

**Background** Acute renal failure (ARF) is a serious complication of critical illness in the ICU. When ARF is severe enough to require renal replacement therapy, mortality approaches 50%. To evaluate interventions to prevent and treat renal failure in medical–surgical critically ill patients, a better understanding of risk factors for ARF in the ICU is needed.
**Objective** To determine the independent baseline and time-dependent risk factors for ARF in a 15-bed medical–surgical closed multidisciplinary ICU in Hamilton, Canada.
**Design** A prospective longitudinal cohort study.
**Population** Consecutive patients admitted to the ICU during 2001 for > 72 hours. Patients were excluded if they had an admitting diagnosis of trauma, orthopedic surgery, cardiac surgery, or pregnancy, or life support withdrawal. We identified all patients requiring hemodialysis as prevalent (within 48 hours of ICU admission) or incident (after 48 hours in ICU) cases of ARF.
**Methods** We recorded 49 potential risk factors for ARF on ICU admission (e.g. pre-existing comorbidities such as diabetes) and daily in the ICU (e.g. exposure to nephrotoxic antibiotics, amphotericin, contrast media, NSAIDS, diuretics and vasopressors). We also recorded strategies to prevent renal failure (e.g. *N*-acetylcysteine before contrast media exposure). We conducted Cox proportional hazard regression analysis to identify patients at risk for ARF.
**Results** Among 261 admissions, 22 patients with chronic renal failure were excluded. Of 239 eligible patients, 11 had missing charts. Of 228 included patients, the mean age was 66.9 (± 15.3) and the mean APACHE II score was 25.2 (± 8.5). Dialysis was initiated within the first 48 hours of ICU admission for nine (3.9%, 95% confidence interval [CI] 1.8–7.4%) patients, and after 48 hours in the ICU for 14 (6.1%, 95% CI 3.4–10.1%) patients. The only independent risk factor for prevalent ARF was being transferred from another ICU (hazard ratio [HR] 5.6 [95% CI 1.0–30.5]). Vasopressors and/or inotropes (HR 18.2 [95% CI 1.5–220.3]) and amphotericin (HR 17.3 [95% CI 2.1–141.6]) were the independent risk factors for incident ARF.
**Conclusions** In this medical–surgical critically ill population, the overall rate of ARF was 10% (prevalence 4%, incidence 6%). Patients at highest increased risk for incident ARF were those transferred from another institution; patients at highest risk for ICU-acquired ARF were those who received vasopressors and/or inotropes, or amphotericin.

## P357

## Clinical features and prognosis of the patients with acute renal failure in the intensive care unit

**T Erdogan, G Erdogan, L Dosemeci, M Yilmaz, M Cengiz, A Ramazanoglu**
*University of Akdeniz, Antalya, Turkey*
*Critical Care* 2005, **9(Suppl 1):**P357 (DOI 10.1186/cc3420)

**Objective** To examine the etiologies of acute renal failure (ARF) and to evaluate the hemodynamic and ventilatory data, mortality, ICU and hospital stays and therapies of the patients with ARF. We compared these parameters between the patients who had ARF at ICU admission and those who developed ARF during their ICU stay.

**Methods** Seven hundred and thirty patients admitted to the ICU from January 2001 to January 2002 were retrospectively evaluated in terms of ARF. A serum creatinine level of 2 mg/dl or more was defined as ARF, and 72 patients were diagnosed as ARF. Among 72 patients with ARF, Group 1 ($n = 47$) consisted of the patients who had ARF at ICU admission. Group 2 ($n = 25$) consisted of the patients who developed ARF during their ICU stay.
**Results** There was no difference in the demographic data and APACHE II scores between the two groups ($P > 0.05$). The mortality rate of the patients who had ARF at ICU admission was 72%. The patients who developed ARF in the ICU had a mortality of 68%. The mean durations of the mechanical ventilation, ICU and hospital stay of the patients in Group 1 and Group 2 were 9.04 ± 10.9 and 9.7 ± 9.04 days, 10.6 ± 13.3 and 12.3 ± 9.6 days, and 20.5 ± 20.6 and 17.5 ± 11.8 days, respectively. There was no significant difference in terms of the mortality rate, ICU and hospital stay, hemodynamic and respiratory data between the two groups ($P > 0.05$). The mean serum creatinine levels were 4.4 ± 2.3 vs 3.2 ± 0.7 mg/dl ($P < 0.01$), and the mean serum lactate levels were 2.17 ± 2.8 vs 0.94 ± 0.9 mmol/l ($P < 0.01$). Hemodialysis was required in 37.5% of all patients with ARF. The most frequent reason causing ARF was sepsis (61%).
**Conclusion** The mortality rate of our critically ill patients with ARF was approximately 70%, which is comparable with the results of the literature. There was no significant difference in terms of mortality and morbidity between patients who had ARF at ICU admission and those who developed ARF during their ICU stay.

### P358

### Renal failure in obstetrics: epidemiology and outcome in the intensive care unit

**Z Haddad, C Kaddour, M Laamourou, T Chaaoua, R Souissi, S Sghaier**
*Neurology, Tunis, Tunisia*
*Critical Care* 2005, **9(Suppl 1):**P358 (DOI 10.1186/cc3421)

**Introduction** Acute renal failure (ARF) is a serious complication of pregnancy. It is associated with an increased mortality.
**Objective** To determine risk factors and outcome of peripartum ARF.
**Design** Demographic and obstetric management (transfusion, cesarean section, hysterectomy, anesthetic complications, etc.) data were collected and analysed. ARF was defined as creatinine levels ≥ 100 µmol/l and/or oliguria <150 ml/8 hours or < 500 ml/day. Generalistic scoring systems (APACHE II, APACHE III) and organ dysfunction scoring systems were calculated at admission and on a daily basis. Data were computed on SPSS 11.5 XP-Windows compatible. Results were expressed as means ± standard deviation. Statistical analysis was based on the chi-squared test and Student *t* test corrected by the Fisher exact test.
**Setting** A multidisciplinary ICU.
**Study period** January 1996–December 2003.
**Patients** Obstetric patients ($n = 541$) admitted in the ICU.
**Measurements and results** The mean age was 31.2 ± 5.9 years, mean term was 34.7 ± 4.5 weeks. The major part of our patients were admitted after delivery. Obstetric complications accounted for 70% of admissions. Pre-eclampsia, eclampsia and peripartum haemorrage were the leading causes associated with ARF. Overall mortality was 10.4% ($n = 57$). ARF was noticed in 68 patients, with a mortality of 33.8% ($n = 23$). The relative risk (RR) of mortality when patients developed ARF was 4.7 with an odds ratio (OR) of 6.6. We distinguished two populations: ARF with (Dial+) ($n = 22$) or without (Dial–) dialysis ($n = 46$); mortality was respectively 10/22 and 13/46. Mean scores for patients with and without ARF were respectively: 41.1 ± 20.9 and 21.6 ± 13.7 for SAPS II; 16 ± 8 and 7.5 ± 6 for APACHE II and 63.3 ± 31.6 and 24.4 ± 23.8 for APACHE III ($P < 0.01$ for all scores). Renal failure was usually associated with at least another organ dysfunction as demonstrated by mean SOFA at day 1 (9.3 ± 4.5) whereas without ARF it was 3.7 ± 3 ($P < 0.001$). Dial+ and Dial– respectively showed an OR concerning mortality of 8.37 and 4.04 and a respective RR of 6.33 and 3.93 compared with patients without ARF. Persistant oliguria was the major cause of dialysis. A cut-off point of creatinine at 300 µmol/l is associated with a RR of mortality of 3.5 compared with patients that developed ARF with lower creatinine levels.
Univariate analysis found that uterine atonia, transfusion, multiple pregnancy and vaginal delivery were significantly associated with ARF, whereas cesarean section showed an OR = 0.455. Multiple regression analysis retained only transfusion prior to ICU hospitalization as significantly associated with ARF. Oliguria and the level of renal failure are predicting factors of mortality.
**Conclusion** ARF is associated with high mortality (> 30%). Aggressive treatment and prevention of renal failure is necessary to improve prognosis.

### P359

### Filtration gradient and abdominal perfusion pressure do not correlate with urinary output in patients at risk for intra-abdominal hypertension and normal serum creatinine

**J De Waele, E Hoste, S Blot, K Colpaert, J Nollet, S Oeyen, C Roosens, J Decruyenaere**
*Ghent University Hospital, Gent, Belgium*
*Critical Care* 2005, **9(Suppl 1):**P359 (DOI 10.1186/cc3422)

**Introduction** In patients with intra-abdominal hypertension (IAH), decreased urinary output is an early sign of renal impairment. The exact mechanisms remain unknown, but decreased perfusion pressure, increased pressure on the venous outflow tract, and increased tubular pressure are possible explanations. Because the abdominal perfusion pressure (APP = MAP – IAP) does not take the increased tubular pressure into account, the filtration gradient (FG = glomerular filtration pressure – proximal tubular pressure = MAP – 2 × IAP) has been proposed as a better reflection of renal pressure gradients.
**Objective** The aim of this analysis was to study the correlation between urinary output (UO) and APP or FG at the individual patient level in patients with normal serum creatinine, and to compare the correlations between FG and UO with APP and UO.
**Methods** We studied 27 surgical ICU patients at risk for IAH. Causes of intra-abdominal hypertension included primary and secondary IAH. Median age was 60 years (IQR 36–74 years), median APACHE II score on admission 13 (IQR 10–19).
IAP was measured transvesically after instillation of 20 ml saline. IAH was defined as a sustained IAP >12 mmHg, according to the World Society of Abdominal Compartment Syndrome guidelines. The APP, FG and UO (expressed as ml/kg/hour) were calculated for each IAP measurement. For each individual patient, the correlation coefficient between urinary output and APP or FG was calculated. When serum creatinine levels were above 1.2 mg/dl or when patients were anuric at the moment of IAP measurements, observations were not taken into consideration for analysis of the correlation between the parameters studied.
**Results** Four hundred and thirty-one paired datasets were available for analysis. Mean IAP in all observations was 13 ± 5.2 mmHg, mean APP 73 ± 16.0 mmHg and mean FG 60 ± 18.7 mmHg. IAH was present in 40% of the observations.

There was no significant correlation between APP and UO in 24/27 patients, and no significant correlation between FG and UO in 23/27 patients. When the correlation was significant for both parameters, FG correlated better with UO than APP in all patients.
**Conclusion** In this sample of critically ill patients with normal serum creatinine and at risk for IAH, there was no correlation at the individual patient level in the majority of the patients. The correlation between FG and UO was better than between APP and UO when there was a significant correlation.

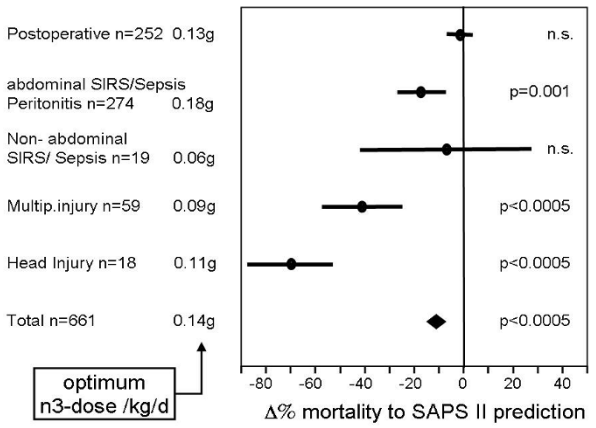
## P360

## Omega 3 fatty acids reduce mortality and length of hospital stay in a cohort of 661 patients with different diagnoses

**A Heller, S Rössler, T Koch**
*University Hospital Carl Gustav Carus, Dresden, Germany*
*Critical Care* 2005, **9(Suppl 1):**P360 (DOI 10.1186/cc3423)

**Background** Supplementation with omega 3 fatty acids (n3PUFA) exerts immune-modulating and organ-protective effects, even after short-term infusion in both postoperative and critically ill patients [1,2]. The aim of this study was to evaluate dose-dependent effects of a fish oil (FO) emulsion on the clinical course of patients with different diagnoses. Primary study endpoint was survival; secondary endpoints were length of hospital stay and use of antibiotics.
**Materials and methods** After approval by the National Board for Drug Safety (BfArM) and the Institutional Ethics Board we analyzed a database containing 661 patients from 82 German hospitals who received total parenteral nutrition (TPN) for at least 3 days. The cohort was divided into five groups according to the administered FO dose (Omegaven, Fresenius Kabi).
**Results** The patients of this survey were 62 ± 17 years old (SAPS II 32 ± 14). Diagnoses and patient numbers are shown in Fig. 1. In multivariate analysis the absolute dose of FO per kg/day had a 2–20 times higher impact on respective outcome parameters than the ratio of n3/n6 PUFA, which is considered to be a major determinant of beneficial n3 effects in the current literature. TPN including FO had most favourable effects on survival, infection rates and length of stay when administered in doses between 0.1 and 0.2 g/kg/day. Diagnosis-related optimum FO doses are given in Fig. 1.
**Conclusion** FO administration may reduce mortality, antibiotic use, and length of hospital stay. Individual optimum FO doses and effect sizes are diagnosis dependent.

**Figure 1 (abstract P360)**




**Acknowledgements** The authors thank R Koch and J Novotny for biomathematical advice.
**References**
1. Gadeck JE, *et al.*: *Crit Care Med* 1999, **27:**1409-1420.
2. Heller AR, *et al.*: *Int J Cancer* 2004, **111:**611-616.

## P361

## Probiotic treatment restores short-term fasting-induced colonic mucosal atrophy in rats

**K Kotzampassi[1], D Paramythiotis[1], A Voudouris[1], E Mioglou[2], Z Iakovidou[2], E Eleftheriadis[1]**
*[1]Department of Surgery, University of Thessaloniki Medical School, Thessaloniki, Greece; [2]Department of Biology, University of Thessaloniki Medical School, Thessaloniki, Greece*
*Critical Care* 2005, **9(Suppl 1):**P361 (DOI 10.1186/cc3424)

**Background and aim** Short-term fasting, although a common prescription perioperatively, has been found to result in metabolic impairment and severe alterations in the morphology and function of the gut. Probiotics have been reported to stimulate epithelial proliferation in the colon and thus might promote restoration of gut mucosa after starvation. The aim of the present study was to investigate the effects of probiotics on improving recovery of colonic mucosal atrophy (expressed by the mucosal DNA content) after short-term fasting in rats.
**Materials and methods** Twenty-four male Wistar rats were fasted for 3 days and then, for the next 3 days, were fed with standard rat chow or rat chow plus probiotics (Synbiotic 2000Forte; Medifarm, Sweden), or given parenteral liquids with or without probiotics orally. Six more rats were normally fed with standard rat chow for 6 days, and served as controls. Synbiotic 2000Forte contains $10^{10}$ CFU of each of *Pediococcus pentoseceus* 5-33:3, *Leuconostoc mesenteroides* 32-77:1, *L. paracasei* ssp paracasei 19 and *L. plantarum* 2362, as well as 2.5 g inulin, oat bran, pectin and resistant starch. At the end of the 3-day refeeding period the entire colon was opened longitudinally, and the mucosa stripped out, weighed and assayed for DNA contents (μg/g tissue).
**Results** Three days' feeding with rat chow plus probiotics or parenteral liquids in combination with per oral probiotics was found to significantly ($P = 0.05$) increase DNA contents in relation to rat chow or parenteral liquids, respectively. However, it is of interest to mention that there is no difference between mucosal DNA contents in rats treated parenteral liquids plus per oral probiotics and rats fed rat chow without probiotics.

**Table 1**

| Rat chow | Rat chow + probiotics | Parenteral | Parenteral + probiotics | No fasting (controls) |
|---|---|---|---|---|
| 3.15 ± 0.98 | 3.79 ± 0.82 | 2.47 ± 0.36 | 3.11 ± 0.53 | 4.91 ± 0.91 |

**Conclusion** The results of the present study led us to conclude that probiotics enhance the recovery of gut mucosa after short-term starvation-induced atrophy in rats.

## P362

### Benefits of Synbiotic 2000 Forte in critically ill patients: a randomized controlled trial

**A Voudouris[1], P Kazamias[2], E Spyridaki[3], A Antonopoulou[3], E Giamarellos-Bourboulis[3], C Skourtis[1], K Kotzampassi[1]**
*[1]Department of Surgery, University of Thessaloniki Medical School, Thessaloniki, Greece; [2]ICU of 424 Military Hospital, Thessaloniki, Greece; [3]Department of Internal Medicine, University of Athens Medical School, Athens, Greece*
*Critical Care* 2005, **9(Suppl 1):**P362 (DOI 10.1186/cc3425)

**Background and aim** Early probiotics administration was suggested to reduce the incidence of infections and thus the overall morbidity and mortality in surgical patients. The aim of this prospective randomized clinical trial was to assess the effects of a combination formula of probiotics and prebiotics (Synbiotic 2000Forte; Medifarm, Sweden) versus prebiotics only (fiber) in critically ill, long-term mechanically ventilated trauma patients.
**Materials and methods** Patients were randomized to either treatment for a 2-week treatment period. Synbiotic 2000 Forte consists of $10^{10}$ CFU of each of *Pediococcus pentoseceus* 5-33:3, *Leuconostoc mesenteroides* 32-77:1, *L. paracasei* ssp paracasei 19 and *L. plantarum* 2362, as well as 2.5 g inulin, oat bran, pectin and resistant starch. Blood samples were collected on days 0, 4, 7 and 15 for measurements of CRP, PCT, MDA, tumor necrosis factor alpha, IL-6. Days under ventilatory support, days of total stay in the ICU, gut motility, antibiotic-associated diarrheas, infections, and septic morbidity as well as overall mortality were also recorded.
**Results** Patients were well matched regarding age and sex distribution, APACHE II and Glasgow scores. From day 7, all patients of the Synbiotic group exhibited a progressive reduction of all inflammatory indexes in relation to the prebiotics only group ($P = 0.05$). Similarly, they had a significantly shorter ICU stay and days on mechanical ventilation ($P = 0.04$), less episodes of antibiotic-associated diarrheas and less distension and cramps after enteral nutrition, in relation to the prebiotics group. The overall infection rate was 34% versus 90%, respectively, while three patients from the prebiotics group died after sepsis and MODS.
**Conclusion** The administration of the Synbiotic 2000 Forte formula in critically ill ventilated trauma patients favorably altered the systemic inflammatory response and seemed to be associated with measurable clinical benefits.

## P363

### The effects of enteral feeding with eicosapentaenoic acid, gamma-linolenic acid and antioxidants in patients with sepsis

**A Pontes-Arruda**
*Hospital Antônio Prudente, Fortaleza, Ceará, Brazil*
*Critical Care* 2005, **9(Suppl 1):**P363 (DOI 10.1186/cc3426)

**Introduction** Nutritional support with diets containing eicosapentaenoic acid (EPA), gamma-linolenic acid (GLA) and antioxidants can improve lung microvascular permeability, oxygenation and cardiopulmonary function, by modulating proinflammatory eicosanoid (leukotriene $B_4$, prostaglandin E, thromboxane $B_2$) production from arachdonic acid [1]. This kind of enteral diet can improve gas exchange and clinical outcomes in comparison with a standard control diet in patients with ARDS [2]. The scope of this study is to investigate whether an enteral diet enriched with EPA, GLA and elevated antioxidants can improve outcomes and reduce all-cause mortality in patients with sepsis.
**Materials and methods** This abstract reports the preliminary results of a prospective, randomized, controlled trial. Thirty patients with clinical diagnosis of either sepsis, severe sepsis or septic shock, and under mechanical ventilation were included in this work and randomized for a high-fat, low-carbohydrate enteral nutrition formula or an enteral diet enriched with EPA, GLA and elevated antioxidants (Oxepa; Abbott Laboratories), isocaloric and isonitrogenous to the control diet, differing only in its lipid composition and level of antioxidant vitamins. The patients received the enteral formula during mechanical ventilation in association with the sepsis standard of care [3]. Enteral feeding was delivered at a constant rate to achieve a minimum of 50% of Basal Energy Expenditure (BEE) (Harris–Benedict equation) × 1.3 within the first 24 hours and, if well tolerated, a minimum of 75% of BEE × 1.3 within 72 hours of initiation of enteral feeding, until the complete weaning from ventilator. At the time of hospital discharge, the patients' charts were reviewed to assess a number of outcome variables. The primary outcome is 28-day all-cause mortality. We perform the statistical analysis of the two dietary groups using a one-way analysis of variance.
**Results** Septic patients fed EPA, GLA and elevated antioxidants maintained higher oxygenation status ($P = 0.001$), more ventilator-free days ($P = 0.001$), more ICU-free days ($P = 0.02$) and lower mortality rates ($P = 0.03$).
**Conclusions** This study suggests that an enteral diet containing EPA, GLA and elevated antioxidants can contribute to better ICU and hospital outcomes of septic patients. This can be through a downregulation on the synthesis of proinflammatory mediators that contributes to restoring homeostasis of the septic patients. The beneficial effects of this diet suggest that this enteral nutrition formula would be a useful adjuvant therapy in the clinical management of sepsis.
**References**
1. Pacht ER, *et al.*: *Crit Care Med* 2003, **31:**491-500.
2. Gadek JE, *et al.*: *Crit Care Med* 1999, **27:**1409-1420.
3. Dellinger RP, *et al.*: *Crit Care Med* 2004, **32:**858-873.

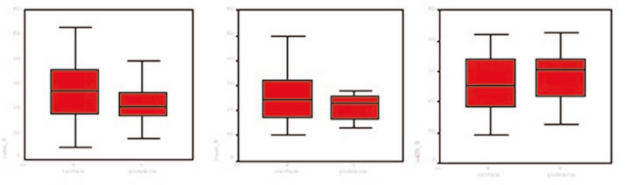
## P364

### Effects of L-alanyl L-glutamine dipeptide-supplemented parenteral nutrition on lymphocyte subpopulations and in prevalence of nosocomial infection in critically ill patients

**P Martins[1], L Alves[2], M Santos Rosa[2], L Lemos[2], P Casanova[1], J Falcão[1], N Devesa[1], J Pimentel[1]**
*[1]University Hospital Coimbra, Portugal; [2]Faculty of Medicine of Coimbra University, Portugal*
*Critical Care* 2005, **9(Suppl 1):**P364 (DOI 10.1186/cc3427)

**Background** In critically ill patients glutamine (GLN) becomes an essential amino acid. Several studies showed a relationship between GLN depletion and the increased nosocomial infection in ICU patients. There are a kinetics profile of lymphocyte activation from early (CD69) to late (CD25 and HLA-DR) cell surface marker expression that relates directly to the ability to mount an effective immune response to infectious agents. The purpose of the present study is to investigate the effects of glutamine-supplemented parenteral nutrition on lymphocyte subpopulations and the kinetics profile of lymphocyte expression markers of activation, and correlate it with the infectious morbidity in critically ill patients.
**Patients and methods** We performed a blind randomised, controlled study of GLN-enriched parenteral nutrition (GLN-PN). Twenty-eight critically ill patients were randomly assigned to two groups of nutrition therapies, as either Dipeptiven® (0.40 g/kg/day) supplemented parenteral nutrition (glutamine group $n = 16$) or an isocaloric and isonitrogenous standard parenteral nutrition

**Figure 1 (abstract P364)**



(standard group $n = 12$). Blood samples were obtained for lymphocyte subpopulations (NK, CD3, CD4, CD8, CD56, CD19, CD25, CD69 and HLA-DR) at the beginning and at the fifth and 10th day after standard TPN. Flow cytometry analysis was performed immediately. Nosocomial infections from entry to discharge from the ICU were determined.

**Results** Baseline data (age, sex and severity score – APACHE II) were similar in the standard and glutamine groups. GLN-PN-treated patients had less nosocomial infections (14 vs 25 nosocomial infectious episodes). The CD4/CD8 ratio showed an increase from day 1 to day 5 in the GLN group. Mean lymphocyte expression activation marker CD69 and HLA-DR are slightly increased at day 5 in the standard group, while the later expression lymphocyte activation marker CD25 is increased in the GLN group (Fig. 1). The mortality in the ICU is increased in the standard group (25 vs 12.5%).

**Conclusions** We conclude that in critically ill patients GLN-PN can reduce the incidence of infectious complications and mortality. This pilot study showed that the GLN-PN supplement improved not only lymphocyte activation, but also regulatory mechanisms of lymphocyte proliferation, illustrated by increased lymphocyte expression surface marker CD25, compared with CD69 and HLA-DR. This effect can apparently decrease nosocomial infections and mortality in ICU patients.

## P365

### Managing diarrhea and fecal incontinence: results of a prospective clinical study in the intensive care unit

**T Gallagher, J Wishin**
*University of Florida College of Medicine, Gainesville, FL, USA*
*Critical Care* 2005, **9(Suppl 1):**P365 (DOI 10.1186/cc3428)

**Introduction** Managing fecal incontinence and diarrhea challenges ICU staff to control the fecal output and to protect the skin. This diverts resources from other vital patient needs. A new medical device system (FMS) was developed in which an inflated balloon retains a tube within the rectum while an external pouch collects fecal material, offering an option for temporary continence in subjects with uncontrolled diarrhea.

**Hypothesis** Safety and performance of an innovative system (FMS) for managing fecal incontinence was evaluated in a prospective non-comparative study in two ICUs.

**Methods** Ten subjects with diarrhea and incontinence in two ICUs had the FMS inserted. Endoscopic proctoscopies of the rectal vault assessed the condition of the anorectal mucosa pre-insertion and post-removal. Investigators assessed ease of FMS insertion and removal, device retention and leakage, patient comfort, perineal skin condition and presence or absence of odor during FMS use.

**Results** The FMS device performed well during use for 1–13 days with no safety issues among any of the 10 subjects, although two died during the study due to non-product-related illnesses. It was judged easy to insert and to remove with easy-to-follow instructions. All subjects retained the device without difficulty or external securing devices for the duration of the study, except one with a weakened internal sphincter who expelled it after 8 hours. During a total of 65 daily assessments, nurses reported the FMS effective and time efficient in managing fecal incontinence, with no odor or discomfort reported and limited leakage. During FMS use, perineal and buttock skin condition was maintained or improved in all but one patient who developed patchy redness on the buttocks.

**Conclusions** The FMS was well accepted, performed well, with no safety issues, for all patients and helped reduce the risk of perineal and buttock skin breakdown.

## P366

### Luminal lactate and tyrosine release during intestinal ischemia in rabbits

**S Lobo, L Contrin, L Navegantes, S Orrico, M Queiroz, P Cury, E Lira, A Carta, A Yamamoto, S Portella, J Vincent**
*Famerp – Hospital de Base, Sao José do Rio Preto, Brazil*
*Critical Care* 2005, **9(Suppl 1):**P366 (DOI 10.1186/cc3429)

**Introduction** The intestinal tract plays a central role in the protein catabolic response after injury and infection. Tyrosine (an index of overall proteolysis) and lactate release were evaluated in luminal gut perfusate during ligation of the superior mesenteric artery (SMA). The aim of this study is to determine whether tyrosine flow from the intracellular compartment to the lumen could occur during ischemia-induced gut injury.

**Methods** Fourteen anesthetized New Zealand rabbits were allocated into two groups (group I: control, $n = 5$ and group II: ischemia, $n = 9$). SMA (QSMA) and aortic (Qaorta) flows were measured using ultrasonic flow probes. A segment from the ileum was isolated using two multilumen tubes with inflated balloons to delimit a closed segment to be perfused. In a second gut segment, a tonometric catheter (TRIP® Tonometry Catheter; Datex, Finland) was placed. Animals in group II were submitted to ligation of SMA after baseline measurements. The concentrations of lactate and tyrosine were determined in serum and gut luminal perfusate (GLP). Tyronise was assayed by the fluorometric method as previously described [1].

**Results** Lactate concentration significantly increased in GLP after ligation of SMA (from 0.15 ± 0.05 mEq/l to 3.5 ± 1.2 mEq/l at 2 hours) in comparison with the control (from 0.18 ± 0.43 mEq/l to 0.22 ± 0.12 mEq/l at 2 hours) ($P < 0.05$). Luminal tyrosine significantly increased during ischemia compared with the control at 2 hours (from 11.9 ± 8.9 mM/ml to 84 ± 22 mM/ml, group II; and from 6.9 ± 2.9 mM/ml to 15.3 ± 13.8 mM/ml, group I; $P < 0.05$).

**Conclusion** Ischemia rapidly induces gut-derived proteolysis in rabbits.

**Reference**

1. Waalkes TP, Udenfriend S: **A fluorometric method for the estimation of tyrosine in plasma and tissues.** *J Lab Clin Med* 1957, **50:**733-736.

## P367

Abstract withdrawn.

## P368

### The impact of gastrointestinal failure on intensive care unit mortality

**A Reintam[1], P Parm[1], U Redlich[2], L Tooding[3], J Starkopf[3], C Spies[4], H Kern[2]**
*[1]Tartu University Clinics, Tartu, Estonia; [2]DRK Kliniken, Berlin, Germany; [3]Tartu University, Tartu, Estonia; [4]Charite Universitätsmedizin, Berlin, Germany*
*Critical Care* 2005, **9(Suppl 1):**P368 (DOI 10.1186/cc3431)

**Objective** To determine the incidence of gastrointestinal failure (GIF) in the ICU and its impact on mortality.
**Methods** A retrospective study on adult patients ($n = 2588$) admitted to three ICUs (two ICUs at Berlin Charité, Germany and one ICU at Tartu University Hospital, Estonia) during the year 2002 was performed. GIF was defined as documented gastrointestinal problems (including food intolerance, gastrointestinal haemorrhage and ileus). The risk ratio (RR) and odds ratio (OR) were calculated to evaluate GIF as a risk factor of death.
**Results** A total of 252 patients (9.7%) developed GIF during the ICU stay. We showed that in patients who develop GIF the risk of death increases remarkably. The most dramatic rise in risk of death occurred in elective cardiosurgical patients in Berlin, with risk ratio 23.4 and OR 31.82. The risk of death rose also in surgical and medical emergency patients (RR 5.5; OR 9.21 in Berlin and RR 3.2; OR 7.67 in Tartu).
By evaluating patients according to their maximum SOFA score, we demonstrated that patients with GIF had lower survival rates compared with nonGIF patients. The incidence of GIF significantly raised the risk of death in patients with SOFAmax <12 ($P < 0.001$; Table 1), while in patients with SOFAmax of 12 or more points differences between the GIF and nonGIF cohorts were not significant.

**Table 1**

| SOFAmax | GIF survival, *n* (%) | NonGIF survival, *n* (%) | OR (95% CI) for death | *P* |
|---|---|---|---|---|
| < 7 | 28 (82.4) | 1711 (99.2) | 26.19 (9.49–72.97) | < 0.001 |
| 8–11 | 54 (73.0) | 404 (89.8) | 3.25 (1.77–5.99) | < 0.001 |
| 12–14 | 49 (66.2) | 70 (70.0) | 1.19 (0.20–2.27) | 0.624 |
| >15 | 11 (15.9) | 10 (30.3) | 0.44 (0.16–1.17) | 0.118 |

**Conclusions** Development of GIF has an impact on ICU mortality. Using GIF together with the SOFA score might be helpful for estimating the risk of death in ICU patients. Further studies are needed for establishing a proper definition of GIF.

## P369

### Incidence of gastrointestinal failure in intensive care unit patients: retrospective and prospective study

**A Reintam[1], P Parm[1], H Kern[2], J Starkopf[1]**
*[1]Tartu University Clinics, Tartu, Estonia; [2]DRK Kliniken, Berlin, Germany*
*Critical Care* 2005, **9(Suppl 1):**P369 (DOI 10.1186/cc3432)

**Objective** To describe the incidence of gastrointestinal failure (GIF) and ICU performance according to GIF in a comparison of two studies.
**Design** A retrospective study of year 2002 and a prospective study in 2004.
**Patients** A total of 468 adult patients of surgical and medical emergency were admitted to the ICU of Tartu University Hospital in 2002 and 201 patients were admitted in 2004. Patients' mean APACHE II score at admission was 13.7 in 2002 and 16.4 in 2004, the mean SOFA score at admission was 6.8 and 6.7 points, respectively. Sixteen percent of patients in 2002 and 19% in 2004 were transferred from other hospitals. A total 20.0% and 17.5%, respectively, were reanimated before admission.
**Measurements** For 2002, data from patients' charts were retrospectively recorded in a computerized database. In 2004 an existing database was used in a prospective manner. In both studies GIF was defined as documented gastrointestinal problems (including food intolerance, gastrointestinal haemorrhage and ileus) in patient data. Comparative analysis was performed with the chi-square test.
**Results** Incidence of GIF was 15.6% in the retrospective study and 29.9% in the prospective study ($P < 0.001$). Patients with GIF had significantly higher mortality, longer ICU stay (Table 1) and longer mechanical ventilation period. Mortality of GIF patients was 67.1% in 2002 and 51.7% in 2004 ($P = 0.051$), while overall mortality was 28.2% versus 24.4% ($P = 0.343$).

**Table 1**

| | GIF alive | GIF dead | NonGIF alive | NonGIF dead |
|---|---|---|---|---|
| Number of patients (%) | | | | |
| 2002 | 24 (32.9) | 49 (67.1) | 312 (79.0) | 83 (21.0) |
| 2004 | 29 (48.3) | 31 (51.7) | 123 (87.2) | 18 (12.8) |
| ICU days, mean ± SEM | | | | |
| 2002 | 15.0 ± 2.3 | 10.8 ± 1.6 | 4.4 ± 0.3 | 3.0 ± 0.7 |
| 2004 | 17.0 ± 3.9 | 8.9 ± 2.3 | 6.0 ± 0.6 | 0.8 ± 0.1 |

**Conclusions** Gastrointestinal failure is a relevant clinical problem with high mortality, prolonged ICU stay and mechanical ventilation. Without special attention, part of the GIF cases remain unnoticed. Development of universal definition and further studies are therefore needed.

## P370

### Effects of dobutamine on hepatic metabolism in paediatric patients evaluated by LiMON®

**C Cecchetti, C Tomasello**
*Hospital Bambino Gesu, Rome, Italy*
*Critical Care* 2005, **9(Suppl 1):**P370 (DOI 10.1186/cc3433)

**Introduction** Multiple organ dysfunction syndrome (MODS) is a major therapeutic challenge for intensive care physicians treating critically ill patients. The mortality rate in MODS still exceeds 50% despite recent improvements in supportive treatment in the intensive care unit. Abnormal perfusion of the liver can persist after resuscitation in critically ill children, leading to hepatic dysfunction. Since systemic haemodynamic measurements provide a poor estimate of splancnic blood flow, specific tools are required to assess the adequacy of tissue perfusion and oxygenation in critically ill children. These tools have allowed detection of splancnic hypoperfusion even in the absence of altered systemic hemodynamics.
**Aim** To evaluate the effects of dobutamine on hepatosplacnic perfusion and hepatocytic clearance in critically ill children.
**Patients and methods** After resuscitation involving volume expansion with NaCl 0.9%, 14 haemodynamically stable patients (median age: 9 years, median weight 28 kg, height 140 cm) were given an infusion of 6 µg/kg/min dobutamine for 1 hour. Hepatocytic clearance was assessed with plasma disappearance rate of

indocyanine green (PDR dye) elimination at basal time (B0) and after 1 hour (B1). All measurements of PDR dye were made before dobutamine infusion and 1 hour after dobutamine infusion. Analgo-sedation was standard with remifentanyl (0.25 µg/kg/min)–midazolam (0.03 mg/kg/hour) and all patients were in mechanical ventilation with standard settings: pressure controlled with peak inspiratory pressure < 20 $cmH_2O$, mean airway pressure 10 $cmH_2O$, PEEP 5 $cmH_2O$.

**Results** In all patients at baseline the PDR dye was: median 28.8% (range: 37–23.09%); PDR dye changed significantly after dobutamine infusion: 35.9% (range: 28.1–49.8%), with an increase in PDR dye of 22.14%. Haemodynamic values showed: baseline PVC median value 5 (range 2–14), mean blood pressure (MBP) 70 mmHg (range 47–84), HR 110 beats/min (range 78–150); after dobutamine infusion PVC median value 6 (range 4–15), MBP 84 mmHg (range 65–96), HR 121 beats/min (range 93–145)

**Discussion** We have used the indocyanine green (ICG) elimination technique to asses hepatic perfusion. This approach relies on the assumption that hepatic elimination of ICG is flow-dependent. Variations in the plasma ICG disappearance rate therefore directly reflect variations in hepatic blood flow. In summary, our preliminary data show that dobutamine increases hepatocytic clearance in critically ill children.

## P371

### Therapeutic application of the molecular adsorbent recirculating system in chronic severe hepatitis patients complicated with multiorgan failure

**X Hu, Y Zhou, Y Zhao, M Liao, M He, M Wang**
*Department of Severe Liver Diseases, Guangzhou No 8 Hospital, Guangzhou, China*
*Critical Care* 2005, **9(Suppl 1):**P371 (DOI 10.1186/cc3434)

**Objective** The aim of this study is to evaluate the therapeutic effectiveness of the molecular adsorbent recirculating system (MARS) in patients with chronic severe hepatitis complicated with multiorgan failure.

**Methods** The present study randomized 82 patients of chronic severe hepatitis complicated with multiorgan failure into a MARS therapy group of 40 patients and the remaining 42 patients of the control group, respectively. One hundred and ten sessions of MARS treatments were performed with an average of 2.75 sessions per patient. All were evaluated clinically by the model for end-stage liver diseases (MELD) and liver function, hemogram, ammonia lever, coagulopathy, BUN and creatinine levels before and after treatment.

**Results** MARS therapy resulted in remarkable improvement of the prognosis assessment model of MELD ($27.1 \pm 2.81$ to $19.5 \pm 3.66$, $P < 0.01$) and finally benefited the improved survival in the MARS group (19/40, 47.5% vs 10/42, 23.8% of the control group, $P < 0.05$), clinically presented in significant therapeutic effectiveness in hepatic encephalopathy or brain edema, renal dysfunction, obstinate ascites as well as reversal development of systematic inflammatory response syndrome and improvement of hemodynamic and respiratory function by selective elimination of accumulated metabolic toxins and management of electrolyte, fluid and acid–base balance with a safe record.

**Conclusions** MARS therapy can be applied safely as preferable liver support for liver failure patients in therapeutic management for complications and multiorgan failure.

## P372

### Control of intra-abdominal pressure in severe acute pancreatitis with continuous hemodiafiltration using a polymethyl methacrylate membrane hemofilter and colloid fluid therapy

**K Matsuda, H Hirasawa, S Oda, H Shiga, M Nakamura, E Watanabe**
*Department of Emergency and Critical Care Medicine, Graduate School of Medicine, Chiba University, Chiba, Japan*
*Critical Care* 2005, **9(Suppl 1):**P372 (DOI 10.1186/cc3435)

**Aim** It is generally accepted that vascular permeability is increased by the pathologic effects of various humoral mediators, leading to reduction of circulating blood volume and fluid collection in the abdominal cavity, or intestinal edema in the early stage of severe acute pancreatitis (SAP). The hyperpermeability-induced patho-physiological conditions thus increase the intra-abdominal pressure (IAP), and eventually cause intra-abdominal hypertension (IAH). IAH causes organ dysfunctions such as respiratory failure, circulatory failure, and renal failure, and such a condition is referred to as abdominal compartment syndrome. If the causative humoral mediators can be removed and the vascular permeability can be normalized, the administration of oncotic agent can increase colloid osmotic pressure (COP) and reduce IAP. We have claimed that continuous hemodiafiltration using a polymethyl methacrylate membrane hemofilter (PMMA-CHDF) can remove various humoral mediators from the blood stream and that PMMA-CHDF and colloid fluid administration can reduce interstitial edema. The present study was undertaken to investigate the efficacy of PMMA-CHDF and colloid fluid therapy for the control of IAP in SAP.

**Patients and methods** Fourteen patients with SAP who were treated with PMMA-CHDF and colloid fluid therapy in the period from May 2000 to December 2003 were included in this study. IAP, COP and the blood level of IL-6 were measured for the initial 3 days. The correlations between the degree of the changes in IAP (dIAP), COP (dCOP), IL-6 (dIL-6) and cumulative water balances (CWB) for the initial 3 days were investigated.

**Results** There was significant and positive correlation between IAP and the blood level of IL-6 before the treatment ($r = -0.75$, $P < 0.01$). There was also significant and negative correlation between the blood level of IL-6 and COP before the treatment ($r = 0.75$, $P < 0.01$). The blood level of IL-6 significantly decreased and COP significantly increased with 3 days of PMMA-CHDF and colloid fluid therapy. IAP also decreased significantly and $380 \pm 2350$ ml water could be removed from the patients for the initial 3 days. There were significant and negative correlations between dCOP and dIL-6, and between dIAP and dCOP ($r = -0.65$, $r = -0.70$, $P < 0.05$). On the contrary, there was no significant correlation between dIAP and CWB.

**Conclusions** These results indicate that IAP significantly correlates with the blood level of IL-6 and COP in patients with SAP, and that PMMA-CHDF and colloid fluid therapy can significantly decrease the blood level of IL-6, increase COP and effectively reduce IAP. We thus conclude that PMMA-CHDF and colloid fluid therapy can control IAP in patients with SAP, and that it should be applied in the early stage of SAP.

## P373

### Impact of abdominal banding on splanchnic organ perfusion

**P Suk, M Masek, M Fencl, V Sramek**
*St. Ann's University Hospital, Brno, Czech Republic*
*Critical Care* 2005, **9(Suppl 1):**P373 (DOI 10.1186/cc3436)

**Introduction** Abdominal banding is still recommended by some surgeons to prevent eventeration after abdominal surgery. We

assessed the impact of increased abdominal pressure (IAP) caused by abdominal banding on perfusion of splanchnic organs, ventilation and hemodynamics.

**Methods** The study protocol was approved by the local EC. Five mechanically ventilated patients after major abdominal surgery were studied. IAP, gastric tonometry ($pCO_2$gap) with a tonometry module (Datex Ohmeda, Finland), plasma disappearance of indocyanine green (ICG-PDR) noninvasively with LiMON (Pulsion Medical Systems, Germany), pulmonary compliance (C-dyn) with a spirometry module (Datex Ohmeda, Finland), hemodynamics and diuresis were recorded (T1). Then IAP was increased by 10 mmHg with an abdominal belt and data measured after 60 min (T2). Then the abdominal bandage was released and a control measurement was done after 60 min (T3). Data are presented as median (range). Friedman analysis of variance was used for statistical analysis and $P < 0.05$ was considered significant.

**Results** IAP increased from 12 (3; 15) to 19 (10; 21) mmHg. After release of banding, IAP decreased to 11 (4; 15) mmHg. $PgCO_2$ increased from 1.61 (1.39; 1.93) kPa (T1) to 2.70 (2; 3.15) kPa (T2) and stayed increased at 2.43 (1.25; 3.10) kPa (T3) (showed a trend). ICG-PDR decreased from 19.1 (7.5; 39.3)%/min to 15.8 (7.7; 20.5)%/min (T2) and increased to 18.2 (6.0; 22.9)%/min (T3) (not significant). C-dyn decreased from 67 (32; 80) ml/cm$H_2O$ to 56 (26; 66) ml/cm$H_2O$ and slightly improved to 59 (32; 70) ml/cm$H_2O$ (showed a trend). HR, MAP, CVP, CO (measured in three patients) and diuresis did not change.

**Conclusion** An increase in IAP caused by abdominal banding can compromise splanchnic organ perfusion and respiratory function in surgical patients.

**Acknowledgement** Supported by IGA of the Czech Ministry of Health 7144-3.

## P374

### A comparison of the effect on gastric emptying of propofol or dexmedetomidine in critically ill patients

**D Memis, D Dokmeci, B Karamanlioglu, A Turan, M Ture**
*Anaesthesiology, Edirne, Turkey*
*Critical Care* 2005, **9(Suppl 1):**P374 (DOI 10.1186/cc3437)

**Background** Propofol and dexmedetomidine are widely used for sedation in the ICU, but there are limited data on the effects on gastric motility. In our study, we were to establish whether or not the propofol and dexmedetomidine effect of gastric emptying is preserved in critically ill patients

**Method** The study involved 24 critically ill, enterally fed adult patients. Each patient received enteral feeding via a nasogastric tube at 50 ml/hour throughout the 5-hour study period – either propofol 2 mg/kg/hour ($n = 12$, Group P) or dexmedetomidine 0.2 µg/kg/hour ($n = 12$, Group D) intravenously over 5-hour infusion. Gastric motility was measured indirectly by analysis of the absorption over time 1.5 g paracetamol administered into the stomach at the start of the study period. At the beginning and end of the study, the residual gastric volume and pH were measured. The rate of gastric emptying is proportional to the area under the line plot of serum paracetamol concentration over 120 min (AUC120).

**Results** The gastric residual volume measured at the end of propofol infusion (11.33 ± 4.84) was found to be higher when compared with the volume measured before infusion (19.33 ± 11.33) and after dexmedetomidine infusion (9.17 ± 4.54). But, there was no difference between groups in the gastric emptying time (AUC 120 894.53 ± 499.39 vs 1113.46 ± 598.09, Group P and Group D, respectively).

**Conclusion** In patients with high gastric residual volume, dexmedetomidine infusion can be the preferred sedative agent.

## P375

### Does diabetes mellitus affect the mortality and morbidity rates after coronary artery bypass surgery?

**Y Bicer, N Yapici, Y Altuntas, F Izgi, O Aydin, Z Aykac**
*Siyami Ersek Thoracic and Cardiovascular Surgery Center, Istanbul, Turkey*
*Critical Care* 2005, **9(Suppl 1):**P375 (DOI 10.1186/cc3438)

**Introduction** Although diabetes mellitus (DM) is one of the major risk factors of developing atherosclerosis, its effects on mortality and morbidity after cardiac surgery are still not clear. We aimed to determine the effects of DM on hospital mortality and morbidity rates.

**Methods** A total of 1245 consecutive patients undergoing coronary artery operations with or without cardiopulmonary bypass from September 2003 to July 2004 were followed to determine risk factors on mortality and morbidity in patients with diabetes and nondiabetes. The statistical analysis was realised by it test for parametric variables and chi-square test for nonparametric variables. $P < 0.05$ was considered statistically significant.

**Results** Twenty percent of all patients were diabetics. According to demographic data and coexisting diseases, there were significant differences between the diabetics and nondiabetics, in sex (female), body mass index (obesity), carotid arterial disease, hypertension, preoperative urea and creatinine levels ($P < 0.001$). Although we found that the inotropic usage of the diabetics were significantly higher ($P < 0.005$), there were no differences in operation, bypass and cross-clamping time between the two groups, In the ICU period, we could not find any difference in intubation time, blood products usage, reoperation and ICU stay. Duration of hospital stay was significantly longer in diabetics ($P < 0.01$). Postoperative complications and mortality rates are presented in Table 1.

**Conclusion** It was interesting to see that although there were no differences in operative and postoperative data between the two groups, factors that could affect the morbidity and the mortality rate were significantly higher in diabetics. In our opinion this was because diabetics unfortunately have more coexisting diseases such as hypertension or renal insufficiency.

**Table 1**

**Postoperative complications and mortality rates**

| Complication | Diabetics (%) | Nondiabetics (%) | *P* value |
|---|---|---|---|
| Stroke | 6 | 0.6 | < 0.001 |
| Renal problems | 6.5 | 2.4 | < 0.001 |
| Total infection | 7.7 | 5.1 | 0.1 |
| Profound surgical site infection | 1.2 | 1.8 | 0.5 |
| Superficial surgical site infection | 3.2 | 1.1 | < 0.001 |
| Mortality | 4.8 | 2.1 | < 0.01 |

## P376

### Hyperglycemia and mortality in high-risk surgical patients

**A Tasiou, M Christodoulou, E Lykoudi, A Vlachou, N Maguina**
*Critical Care Department, Konstantopoulio General Hospital Agia Olga, Athens, Greece*
*Critical Care* 2005, **9(Suppl 1):**P376 (DOI 10.1186/cc3439)

**Introduction** Hyperglycemia and insulin resistance are common in critically ill patients, even if they have not previously had diabetes mellitus. Maintenance of normoglycemia with insulin reduces mortality and morbidity of critically ill patients.

**Study objective** To investigate the relationship between hyperglycemia and intensive care mortality in a group of surgical critically ill patients.
**Methods** We prospectively studied 21 patients (seven females, 14 males, aged 66 ± 14 years old) admitted to a general ICU after high-risk non-cardiac surgery. The exclusion criteria were: known prior diabetes mellitus requiring insulin therapy and hemodynamic instability before or during surgery and during the first hour after admission to the ICU. Demographic data, serum chemistries, type of operation, length of ICU stay (LOS) and mortality were recorded. APACHE II score, blood glucose levels (minimum and maximum levels), $PaO_2/FiO_2$ ratio, heart rate and mean arterial pressure were recorded upon admission to the ICU.
**Results** Non-survivors ($n = 4$) had higher minimum blood glucose levels (217 ± 69 mg/dl vs 128 ± 46, $P < 0.005$) and higher maximum blood glucose levels (270 ± 120 mg/dl vs 192 ± 61 mg/dl, $P < 0.05$) compared with the survivors ($n = 17$). The ICU LOS (17 ± 11 days vs 4 ± 3 days, $P < 0.001$) and days of mechanical ventilation (17 ± 11 days vs 3 ± 3 days, $P < 0.001$) were longer for non-survivors compared with survivors. The APACHE II score on admission was higher for non-survivors than for survivors (22 ± 4 vs 15 ± 9, $P < 0.05$). Non-survivors ($n = 4$) had similar $PaO_2/FiO_2$ ratio levels (202 ± 172 mmHg vs 234 ± 99 mmHg in survivors, $P$ = non-significant). There was no statistically significant difference in mean arterial pressure and heart rate.
**Conclusion** Elevated blood glucose levels during the first 24 hours of the ICU stay are associated with a higher mortality rate in stable surgical patients.

## P377

### Admission hyperglycemia increases mortality in burns

**A Messaadi, K Bousselmi, T Lahouali, S Oueslati**
*Aziza Othmana Hospital, Tunis, Tunisia*
*Critical Care* 2005, **9(Suppl 1):**P377 (DOI 10.1186/cc3440)

**Introduction** Stress hyperglycemia is a common event in acute critical illness. Hyperglycemia may contribute to morbidity and mortality after burns. The purpose of this study was to assess the incidence of admission hyperglycemia in burn patients and its repercussion on mortality rates.
**Patients and methods** A survey of the medical records from January 2000 to January 2004 identified 855 patients. Only unknown diabetic patients with admission blood glucose levels >1.4 g/l were considered. The group of hyperglycemia patients (H+) was compared with a control patient group deemed to have normal glucose level and the same epidemiological data (H–). Data analysis was performed with EpiInfo software
**Results** Admission hyperglycemia was observed in 8.6% of patients (74/855 admissions). Only 15 patients had the benefit of insulin therapy. Epidemiological characteristics and gravity scores where similar in the two groups, H+ and H–, as shown in Table 1. The mortality rate in group H+ (46%), however, was significantly higher than in group H– (28.4%), $P = 0.04$.

**Table 1**

| | H+ ($n = 74$) | H– ($n = 74$) | $P$ |
|---|---|---|---|
| Age | 43 ± 19 | 43 ± 20 | 0.9 |
| Sex ratio | 1.15/1 | 1.15/1 | |
| TBSA | 39 ± 24 | 36 ± 25 | 0.24 |
| ABSI | 8 ± 2.6 | 7.8 ± 3 | 0.34 |
| I BAUX | 83 ± 27 | 81 ± 25 | 0.7 |
| UBS | 94 ± 70 | 82 ± 25 | 0.28 |

**Conclusion** Admission hyperglycemia was observed in 8.6% of our patients. It is a bad prognosis factor in burn patients. Only an aggressive insulin therapy allowing a strict control of blood glucose level can reduce the mortality rate in this group.

## P378

### Intensive insulin therapy does not change the inflammatory response in non-diabetic patients undergoing elective coronary artery bypass grafting

**C Hoedemaekers, P Pickkers, M Netea, M van Deuren, J van der Hoeven**
*University Hospital Nijmegen, The Netherlands*
*Critical Care* 2005, **9(Suppl 1):**P378 (DOI 10.1186/cc3441)

**Introduction** Strict control of plasma glucose in diabetic and non-diabetic patients has been shown to improve outcome in several clinical settings. A large randomized trial in critically ill patients treated with intensive insulin therapy resulted in a 42% reduction in mortality compared with conventional treatment. In patients with acute myocardial infarction, maintenance of blood glucose levels below 11.9 mmol/l has been shown to increase the success rate of thrombolysis, to preserve myocardial function and to improve long-term outcome. There is extensive evidence that glucose can stimulate the production of proinflammatory cytokines such as tumour necrosis factor (TNF) and IL-6, with no effect on the anti-inflammatory cytokine IL-10. We hypothesized that strict glucose regulation results in modulation of cytokine production, resulting in a change in cytokine balance from a proinflammatory state to a more balanced anti-inflammatory condition.
**Methods** We performed a randomized, controlled study in 20 non-diabetic patients undergoing elective coronary bypass surgery. Cardiopulmonary bypass increases proinflammatory and anti-inflammatory cytokines and is associated with the development of SIRS. After surgery patients were randomly assigned to intensive insulin therapy (to maintain blood glucose between 4.4 and 6.1 mmol/l) or conventional insulin therapy (only instituted when blood glucose exceeded 11.1 mmol/l). At 0, 1, 2, 4, 8, 12, 16, and 24 hours after admission to the intensive care unit, plasma samples and samples from the tubes draining the mediastinal cavity were drawn. In these samples levels of the proinflammatory cytokines TNF and IL-6 and the anti-inflammatory cytokine IL-10 were measured by ELISA.
**Results** Both patient groups were comparable with respect to demographics, clinical characteristics and operative data. In the intensive treatment group glucose levels were significantly lower compared with the conventionally treated group. The cumulative insulin dose was significantly higher in the intensive therapy group. No differences were found in levels of TNF, IL-6 and IL-10 in plasma samples or in fluid draining the mediastinal cavity between both groups. Levels of IL-6 and IL-10 were significantly higher in mediastinal fluid samples compared with plasma samples, suggesting a compartmentalized production of cytokines. No differences in TNF levels between plasma and mediastinal fluids were found.
**Conclusions** The protective effect of intensive insulin therapy in critically ill patients is not related to a change in cytokine balance from a proinflammatory to an anti-inflammatory pattern. Systemic cytokine levels are not representative measures for local inflammatory processes.

## P379

### Blood glucose control during cardiac surgery: an evaluation of a fixed versus a variable insulin regime

**A Vohra, A Chan, N Odom**
*Manchester Royal Infirmary, Manchester, UK*
*Critical Care* 2005, **9(Suppl 1):**P379 (DOI 10.1186/cc3442)

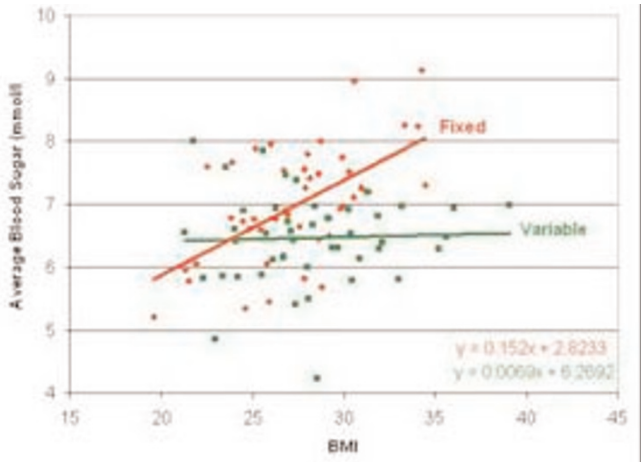
**Introduction** Intensive insulin therapy (blood glucose < 6.1 mmol/l) may reduce mortality after cardiac surgery (by 42%) [1]. An effective regime would keep blood glucose < 6 mmol/l for 80% of the time; < 8 for 90% of the time and <12 for 99% of the time, and no hypos (< 3.0).

**Method** Ninety elective heart surgery patients were recruited, and randomly allocated a 'Fixed' regimen (F) (Table 1) or a 'Variable' regimen (V) (Table 2) ($n = 45$). Blood sugars were recorded 1–2 hourly postoperatively for 48 hours. In each patient the mean and standard deviation were calculated. Episodes of hypoglycaemia (< 3 mmol/l), and mild (6.1–8.0), moderate (8.1–12) or severe (>12) hyperglycaemia were identified.

**Table 1 (abstract P379)**

| Blood sugar (mmol/l) | Infusion rate (IU/hour) | Additional bolus (units) |
|---|---|---|
| < 4.0 | 0 | 0 |
| 4.1–6.9 | 1 | 0 |
| 7.0–8.9 | 2 | 0 |
| 9.0–11.9 | 3 | 5 |
| >12 | 4 | 10 |

**Figure 1 (abstract P379)**




**Results and conclusion** The variable better controlled blood glucose (V = 6.5 ± 0.74; F = 7.0 ± 0.90) ($P = 0.004$) especially in patients with a high BMI (> 25) (Fig. 1). There were more hypos in F ($n = 4$) than V ($n = 1$). Glucose < 6 mmol/l was found for 33% of the time in F, 48% in V; < 8 mmol/l for 75% in F and 82% in V; <12 mmol/l for 99% in F and 99% in V.

**Reference**

1. Van den Berghe G, *et al.*: **Intensive insulin therapy in the critically ill patients.** *N Engl J Med* 2001, **345:**1359-1367.

## P380

### Accuracy of blood glucose measurements in the intensive care unit

**F Staric, U Kovacic, B Ozek, R Kaps**
*General Hospital Novo Mesto, Slovenia*
*Critical Care* 2005, **9(Suppl 1):**P380 (DOI 10.1186/cc3443)

**Introduction** Strict glucose control in critically ill patients may improve survival. According to the Van den Berghe protocol frequent glucose measurements are needed. In the original protocol, however, measurements are made by a blood gas analyzer that is not accessible to our unit. Measurements in the core chemistry laboratory are time and staff consuming and unpractical because of a time delay of about half an hour. According to some other protocols, bedside glucometry is a proposed solution, which is easily accessible and not time consuming. In our preliminary phase of adopting the aforementioned protocol we observed some clinically suspected cases of hypoglycemia, which were not confirmed by the bedside glucometry. However, glucose measurements in the core laboratory confirmed our suspicion. The question arouse whether bedside glucose measurements are accurate enough to be performed in so strict a protocol as that of Van der Berghe.

**Methods** The blood samples were obtained by arterial line. Capilary blood was taken simultaneously. Analysis was performed by the core chemistry laboratory in arterial plasma as the gold standard (GS). Arterial whole blood and capillary blood samples were analysed by four bedside glocometers: Accu-Chek Active (ACA), Accu-Check Inform (ACI), HemoCue (HC) and Gluco Touch (GT). Results were compared with the GS and presented as the correlation coefficient. Data were expressed as the percent of difference to GS and the precision for each glucometer was expressed as the percent of data in the range of ± 10%. The proportion of overestimated values was calculated for each group and the difference between the groups was evaluated by chi-square test. The average percent of difference to GS for all overestimated values for each group was calculated and expressed as the mean ± SD. The difference between the groups was tested by analysis of variance.

**Results** One hundred and forty series of measurements were performed from blood samples of four male and four female critically ill patients. The correlation coefficients and the precision as already defined for each group (a – arterial, c – capillary) were: ACAa – 0.91 and 53%; ACIa – 0.96 and 93%; HCa – 0.91 and 44%; GTa – 0.93 and 13%; ACAc – 0.91 and 2%; ACIc – 0.94 and 91%; HCc – 0.91 and 42%; GTc – 0.85 and 25%. The proportion of overestimated values for ACAa, ACIa and HCa were 27%, 30% and 23%, respectively, and this was significantly less

**Table 2 (abstract P379)**

| Blood sugar (mmol/l) | Start rate (IU/hour) | Sugar falling > 2/hour | Sugar fall 0.5–2/hour | Sugar stable | Sugar rising > 0.5/hour |
|---|---|---|---|---|---|
| > 9.1 | 4 | No change | No change | Increase by 50% | Double rate |
| 6.6–9.0 | 2 | Decrease by 30% | No change | Increase by 50% | Increase by 50% |
| 5.1–6.5 | 1 | Decrease by 50% | Decrease by 30% | No change | Increase by 50% |
| 3.0–5.0 | 0 | Decrease by 80% | Decrease by 50% | Decrease by 30% | No change |

than in the GTa group (98%, $P < 0.05$). The average percent of difference to the GS of all overestimated values in groups ACAa and GTa were 16 ± 15% and 30 ± 20%, which is significantly greater than in groups HCa and ACIa (4 ± 3% for both; $P < 0.05$).
**Conclusion** In the settings where measurements by blood gas analyzers are not possible and core chemistry laboratory data have an unacceptable time delay, AccuCheck Inform measurements are accurate enough to be performed in strict protocols. HemoCue seems also to be acceptable because of its low probability of overestimating the glucose level. The other two analyzers proved to be inaccurate. The best way to obtain a blood samples is an arterial line; however, one should be aware of physiologic and analytic reasons for discrepancy between results from plasma and whole blood samples. Capillary blood sampling is inaccurate, especially in circumstances such as septic shock.

## P381

## Evaluation of intensive insulin therapy

**J Cordingley, S Kemp, A Elia**
*Royal Brompton Hospital, London, UK*
*Critical Care* 2005, **9(Suppl 1):**P381 (DOI 10.1186/cc3444)

**Introduction** Intensive insulin therapy has been shown to improve outcomes in critically ill patients [1]. We evaluated a protocol aimed at achieving a blood glucose concentration of 4–6 mmol/l [2] in patients in an adult cardiothoracic intensive care unit.
**Methods** Records of 552 consecutive patient admissions over a 6-month period were reviewed and compared with 523 patients admitted over a similar time prior to introduction of the protocol.
**Results** Age (median 64 years), sex and APACHE II scores (median 12) and reasons for admission were not significantly different between the groups. Use of intravenous insulin infusions increased from 57% to 87% of patients ($P < 0.01$) and median insulin infusion rate increased from 0.4 to 1.6 units/hour ($P < 0.01$). The mean glucose concentration decreased from 8.3 to 7.2 mmol/l ($P < 0.01$) and the hyperglycaemic index [3] decreased from 2.2 to 1.1 mmol/l.
Intensive care length of stay decreased from 1.8 to 1.0 days (median, $P < 0.01$). Intensive care mortality was not significantly different (4.2% [post] vs 5.2% [pre], $P > 0.05$). There were no significant differences in requirements for blood transfusion, use of inotropes, haemofiltration or the number of patients with bilirubin concentration > 32 μmol/l. The area under the curve for C-reactive protein concentrations corrected for length of stay was significantly lower in the intensive insulin protocol group (89.6 vs 62.0 mg/l, median, $P < 0.01$).
**Conclusion** The mean glucose concentration was not in the target range despite a significant increase in insulin administration. In this observational study the use of an intensive insulin protocol was associated with decreased C-reactive protein concentrations and shorter intensive care unit length of stay. Tighter control of glucose concentrations may be necessary to achieve other previously described benefits of intensive insulin therapy [4].

**References**

1. Van den Berghe G, *et al.*: **Intensive insulin therapy in critically ill patients.** *N Engl J Med* 2001, **345:**1359-1367.
2. Laver S, *et al.*: **Implementing intensive insulin therapy.** *Anaest Int Care* 2004, **32:**311-316.
3. Vogelzang M, *et al.*: **Hyperglycaemic index as a tool to assess glucose control: a retrospective study.** *Crit Care* 2004, **8:**R122-R127.
4. Van den Berghe G, *et al.*: **Outcome benefit of intensive insulin therapy in the critically ill: insulin dose versus glycaemic control.** *Crit Care Med* 2003, **31:**359-366.

## P382

## Intensive insulin therapy in the intensive care unit: assessment by continuous glucose monitoring

**C De Block[1], P Rogiers[2], B Manuel y Keenoy[1], K Bervoets[2], M Smet[2], L Van Gaal[1]**
*[1]University of Antwerp, Belgium; [2]General Hospital Middelheim, Antwerp, Belgium*
*Critical Care* 2005, **9(Suppl 1):**P382 (DOI 10.1186/cc3445)

**Background** Intensive insulin therapy to keep glycaemia at 80–110 mg/dl reduced mortality and morbidity in a surgical ICU. It is not known whether these findings are applicable to a medical ICU. Continuous glucose monitoring (CGM) might improve adjustment of insulin therapy.
**Aims** To assess whether insulin regimens (subcutaneous [s.c.] vs intavenous [i.v.]), based on discontinuous glucose monitoring, are adequate in achieving euglycaemia in a medical ICU. Secondary outcome measures were the influence of glycaemia on inflammatory, renal, and metabolic parameters.
**Methods** So far, 28 patients (male/female: 16/12, mean age 64 ± 16 years, non-diabetic/type 2 DM/type 1 DM: 16/9/3, i.v. vs s.c. insulin: 13/15; median APACHE II score: 20, range 12–32, SOFA score 6 [2–15]; 10 septic shock patients) were recruited in a single-center, prospective, observational study. Forty-eight-hour CGM was initiated within 3 days after admission at ICU, using a subcutaneous glucose sensor (GlucoDay®; Menarini Diagnostics) and compared with arterial blood glucose samples.
**Results** During 48-hour continuous monitoring, glycaemia was >140 mg/dl in 37 ± 28% of the time, and < 60 mg/dl in 5 ± 10% of the time. Target glycaemia (80–110 mg/dl) was reached in only 25 ± 16% of the time. The mean insulin dose per day was 72 units (range 0–276). Patients on s.c. insulin spent more time at glycaemia >110 mg/dl (70 ± 27% vs 47 ± 16% on i.v. insulin, $P = 0.016$), but similar time at glycaemia < 60 mg/dl. Patients with septic shock had higher insulin needs (119 ± 90 vs 46 ± 55 units/day, $P = 0.013$), and tended to spend less time at glycaemia >110 mg/dl (47 ± 22 vs 66 ± 25%, $P = 0.062$). Diabetic patients spent more time at hyperglycaemia (%time >140 mg/dl: 51 ± 27 vs 26 ± 24%, $P = 0.019$). Patients who died at ICU had a higher SOFA score (9 ± 4 vs 6 ± 3, $P = 0.027$), a higher lactate ($P = 0.003$), a higher ferritin ($P = 0.043$), a lower total protein concentration ($P = 0.023$), but similar glycaemic profiles (% time > 200, >140, >110, < 80 and < 60 mg/dl) and insulin dose. Presence of diabetes, insulin regimen and dose did not influence mortality. Glycaemia correlated with leucocyte count ($r = 0.37$, $P = 0.05$), total protein concentration ($r = 0.37$, $P = 0.049$), but not with renal and liver parameters. CGM detected peaks (e.g. when starting total parenteral nutrition) and dales of glycaemia much earlier than discontinous monitoring. CGM data correlated with arterial blood glucose. There were no adverse events with the use of the GlucoDay®.
**Conclusions** The GlucoDay® system, a good method to monitor glucose excursions in ICU patients, was well tolerated. Continuous glucose monitoring is mandatory for optimal titration of insulin therapy in the ICU, as target glycaemia (80–110 mg/dl) was only reached in 25% of the time. An i.v. insulin therapy is better than a s.c. regimen to obtain target glycaemia.

## P383

### Insulin sensitivity and hepatic glucose production in sepsis

**M Zourek, Z Jankovec, Z Rusavy, I Novak**
*University Hospital Charles University, Plzen, Czech Republic*
*Critical Care* 2005, **9(Suppl 1):**P383 (DOI 10.1186/cc3446)

**Introduction** We designed our pilot study to determine to what extent insulin influences carbohydrate metabolism and the associated thermogenesis in septic patients.
**Methods** Five septic patients complying with the inclusion criteria (clinical, laboratory and haemodynamical signs of sepsis having positive blood cultures) underwent the study procedure. Illness severity was assessed using the APACHE II scoring system. Exclusion criteria were hemodynamic instability treated by administration of catecholamines and cortisol, changes in pH and lactate level, hemodialysis or CVVHD.
The glucose rate of appearance (RA) was determined using the stable isotope technique [6,6-2H2]-glucose, and tracer/tracee ratio was measured by gas chromatography–mass spectrometry (GCMS). A priming dose followed by a constant infusion of stable isotope was used to maintain stable plasma enrichment. Basal plasma glucose enrichment was measured after 3 hours of the baseline period. Two step insulin clamps each with 120-min duration were performed using a primed continuous regular insulin infusion. This provided a steady-state infusion rate of 250 IU/min/$m^2$ for the first step, and a five times higher infusion rate for the second step. Arterial blood glucose concentration was maintained at 5 mmol/l. There were taken seven blood samples at 5-min intervals for assessment of the average glucose enrichment before the end of each clamp. A continuous recording of the indirect calorimetry was performed using a Deltatrac II throughout the baseline period of 60 min and for all steady-state periods of clamps (last 40 min of each clamp step).
**Results** Statistical analysis was not performed due to the low number of patients. Results are expressed as mean ± standard deviation at basal conditions versus steady state of each clamp. Total glucose disposal (mg/kg/min): was not calculated vs 2.57 ± 1.05 vs 4.25 ± 1.98, hepatic glucose production (mg/kg/min): 2.48 ± 0.69 vs 0.31 ± 0.53 vs 0.66 ± 0.47, energy expenditure (kJ/min): 8.23 ± 0.95 vs 8.52 ± 0.96 vs 8.99 ± 0.98, glucose oxidation (mg/kg/min): was not calculated vs 1.08 ± 0.94 vs 2.69 ± 1.45.
These preliminary data show that basal gluconeogenesis decreases in septic patients (in comparison with healthy people – literature). Further decrease of hepatic glucose production is present during both clamps, but it is not completely diminished in spite of hyperinsulinaemia.
**Conclusion** Hyperinsulinaemia in septic patients does not completely suppress hepatic glucose production, and glucose remains the main energy substrate in sepsis.

## P384

### Insulin signaling in critical illness: intensive versus conventional insulin therapy

**L Langouche, S Vander Perre, P Wouters, G Van den Berghe**
*Katholieke Universiteit Leuven, Belgium*
*Critical Care* 2005, **9(Suppl 1):**P384 (DOI 10.1186/cc3447)

Insulin resistance and hyperglycemia are common in critical illness. We recently demonstrated that strict maintenance of normoglycemia with intensive insulin therapy during intensive care reduced morbidity and mortality of surgical ICU patients [1]. Little is known, however, about insulin signaling in critical illness. There are two main insulin signaling pathways: the metabolic IRS-phosphatidylinositol-3-kinase (PI3K) pathway, which is impaired in type 2 diabetes, and the mitogenic MAPK pathway. The aim of the present study is to examine the effect of intensive insulin therapy on insulin signaling.
A random selection of 36 non-survivors, who had been randomized to intensive (normoglycemic) or conventional (hyperglycemic) insulin therapy, was comparable for age and severity, duration and type of critical illness. The mean blood glucose levels were 5.6 ± 0.4 and 9.9 ± 0.9 mmol/l ($P < 0.001$) on a median daily insulin dose of 44.2 and 14.4 IU ($P = 0.005$), respectively. Snap-frozen postmortem liver and skeletal muscle biopsies were homogenized and protein levels of signaling molecules were quantified with immunoprecipitation (IRS1 + PI3K and SHC + Grb2), western blotting (phosphorylated Akt) and ELISA (phosphorylated p42/44MAPK).
In the muscle and liver, intensive insulin therapy significantly stimulated the association of IRS with the p85 subunit of PI3K as compared with conventional therapy. The phosphorylation of the downstream signaling molecule Akt was increased in the muscle but not in the liver. To study the effect of intensive insulin therapy on the MAPK pathway, we measured the association of SHC with Grb2 and the phosphorylation of the downstream activator p42/44 MAPK. The two therapy groups did not differ in the amount of associated SHC-Grb2, in neither the muscle nor the liver. There was also no detectable difference in phosphorylated p42/44 MAPK levels.
In conclusion, metabolic insulin resistance in the critically ill, as revealed by an impaired PI3K pathway, can be overcome with intensive insulin therapy in skeletal muscle but not in the liver. Interestingly, liver insulin resistance is associated with an impaired activation of Akt, but not its upstream regulator PI3K. The MAPK pathway is not activated by intensive insulin therapy. Whether unresponsiveness of the mitogenic signal transduction is due to maximal stimulation of this pathway via other signals during critical illness is being explored.

**Reference**

1. Van den Berghe G, *et al.*: *N Engl J Med* 2001, **345:**1359.

## P385

### Influence of blood glucose-related factors to glucose tolerance in acutely ill severe patients evaluated by means of bedside-type artificial pancreas

**M Hoshino[1], Y Haraguchi[2], I Mizushima[1], H Ueno[1], C Tanaka[1]**
*[1]Tokyo Police Hospital, Tokyo, Japan; [2]National Hospital Tokyo Disaster Medical Center, Tokyo, Japan*
*Critical Care* 2005, **9(Suppl 1):**P385 (DOI 10.1186/cc3448)

**Purpose** To verify the importance of the role of blood glucose (BG)-related factors to glucose tolerance in acutely ill severe patients with glucose intolerance.
**Materials and methods** Thirty-four patients in whom BG levels were controlled by means of a bedside-type artificial pancreas (STG-22; NIKKISO Corporation, Japan) were investigated. The target of BG control by STG-22 was set to 150 mg/dl. Glucose tolerance was evaluated by the following five parameters: M value (mg/kg/min), glucose disposal rate measured by the glucose clamp method (GC) using STG-22; M/I value (ml mg/kg/min/mU), M value divided by the blood insulin level (I), which indicates insulin sensitivity; daily mean BG level (BGm) (mg/dl); I/E ratio, the amount of administered insulin from STG-22 divided by administered energy (glucose) (mU/kcal); and insulin clearance (IC) (ml/kg/min), measured by GC with a two-step insulin infusion rate (IIR). GC was performed with a clamped BG level of 80 mg/dl

and IIR of 1.12 and 3.36 mU/kg/min. M1, M3 and I1, I3 indicate the M value and I value when IIR is 1.12 and 3.36, respectively (normal value of M1: 5–10). the first measurement of GC was performed in acute conditions for all the patients, and the second measurement was done 1 week after the first measurement for 20 patients. Organ dysfunction and endogenous insulin production were evaluated by SOFA score and blood C-peptide reactivity (CPR), respectively. Nutritional support for all the patients was performed with total parenteral nutrition. Patients were classified in four groups (A, B, C and D) according to M1 and BGm. Patients with decreased M value (M1 < 5) were subdivided into two groups (A [$n$ = 23], increased BGm, 165 < BGm; B [$n$ = 11], BGm <165). Patients with normal M value (5 < M1) were subdivided into two groups (C [n = 14], BGm <165; D, 165 < BGm).

**Results** (1) The BGm and I/E ratio in group A versus group B were 184 ± 15 vs 150 ± 15 and 51 ± 22 vs 24 ± 18 ($P$ < 0.005), respectively. However, there was no significant difference between group A and group B in the amount of administered glucose, SOFA score, M value (M1, M3), M/I value (M1/I1, M3/I3), IC, and CPR. (2) The BGm and I/E ratio in group C versus group D were 142 ± 19 vs 172 ± 12 and 13 ± 11 vs 50 ± 46 ($P$ < 0.01), respectively. However, there was no significant differences between group C and group D in the amount of administered glucose, SOFA score, M value (M1, M3), M/I value (M1/I1, M3/I3), IC, and CPR.

**Interpretation** There was discrepancy between the M value and BGm, I/E ratio in group B and group D. The M value was measured under a BG level of 80 mg/dl, while the target of the BG control was set to 150 mg/dl. Therefore, the influence of BG-related factors (BG itself or some factors closely related to BG – ex. function of glucose transporter-2) to glucose tolerance was considered in both group B and group D (increased [decreased] glucose metabolism by those factors in group B [group D]).

**Conclusions** BG-related factors seem to have a significant role for glucose tolerance. The artificial pancreas, STG-22, was considered to be useful not only for BG control, but also for further understanding and evaluation of complicated glucose metabolism in acute severely ill patients.

## P386

### Randomized controlled study for the evaluation of automated blood glucose control in critically ill patients

**J Plank[1], M Ellmerer[1], W Toller[1], B Rigler[1], A Amegah-Sakotnik[1], R Hovorka[2], M Willinskaja[2], O Agbaje[1], A Plasnik[1], L Schaupp[3], T Pieber[1]**

*[1]Medical University Graz, Austria; [2]University of Cambridge, UK; [3]Joanneum Research, Graz, Austria*

*Critical Care* 2005, **9(Suppl 1):**P386 (DOI 10.1186/cc3449)

**Introduction** Numerous guidelines have been developed and tested to implement tight glycaemic control in intensive care units. However, most of these guidelines still require user interventions and/or intuitive decisions of intensive care unit staff and do not allow the establishment of an automated glycaemic control system. To develop Closed Loop Insulin Infusion for Critically Ill Patients (CLINICIP), the objective of the present study was to perform a randomised controlled trial testing a fully automated algorithm for the establishment of tight glycaemic control in critically ill patients and to compare the results with routine treatment of glycaemia.

**Methods** In a randomized controlled fashion, 20 patients were included into the trial. Patients were investigated after cardiac surgery and for a period of up to 48 hours. Ten patients were treated according to routine care of glycaemia (change of insulin infusion rate according to actual glucose concentration in 1–4 hourly intervals) or using the fully automated model predictive control (MPC) algorithm as implemented on a laptop computer with hourly adjustment of the insulin infusion rate according to information from blood glucose measurements and under consideration of enteral and parenteral carbohydrate infusions. The glucose target range for both treatments was defined between 80 and 110 mg/dl. In all patients, hourly arterial blood gas analysis was performed and intravenous insulin regimen was adjusted according to general routine care or MPC algorithm, respectively. Analysis according to the last value carried forward was applied as not all patients could be investigated for a period of 48 hours.

**Results** Glucose concentrations, after start of glycaemic treatment, were comparable between both groups (routine care: 136 ± 35 mg/dl; MPC: 147 ± 32 mg/dl; mean ± standard deviation [SD], not significant). No hypoglycaemic event (blood glucose < 54 mg/dl) occurred in either group of the patients and none of the experiments in the MPC group had to be terminated because of a malfunction of the algorithm. During routine care treatment an average blood glucose concentration of 145 ± 31 mg/dl (mean ± SD) was measured. Average glucose concentration were clearly lower in the MPC group with 109 ± 25 mg/dl (mean ± SD). Confirming this result, 9.8% of the glucose measurements as obtained using routine care compared with 51.6% of the glucose concentrations as obtained using MPC treatment were within the glycaemic target range.

**Discussion** These findings suggest that the software algorithm MPC allows save implementation of tight glycaemic control in postcardiac surgery critically ill patients.

## P387

### Implementation of intensive insulin therapy improves glycaemic control in patients managed with conventional insulin therapy

**C Krieger, G Dempsey, T Jones**

*University Hospital Aintree, Liverpool, UK*

*Critical Care* 2005, **9(Suppl 1):**P387 (DOI 10.1186/cc3450)

**Introduction** The implementation of intensive insulin therapy in the critically ill has recently been shown to improve morbidity and mortality [1,2].

**Patients and methods** We have performed a prospective observational study to assess the effects, on all patients, of the first 6 months of an intensive insulin therapy protocol. We have studied 91 patients staying in critical care > 48 hours. This extended to 1233 patient-days and 7987 individual sugar estimations. For intensive insulin therapy blood sugars were maintained between 4 and 7 mmol/l.

**Results** Fifty-two patients received intensive insulin therapy during their admission, 39 did not. The demographics of the two groups were well matched. The impact of the institution of the protocol was assessed in two 3-month blocks. The mean blood glucose in the intensive insulin therapy group was significantly lower than the conventional therapy group ($P$ < 0.0001, unpaired $t$ test). Glycaemic control failed to improve in the second 3 months in the intensive therapy group (Table 1). There was a significant reduction in blood sugars in the second 3 months for conventional control (Table 1).

**Conclusions** Intensive insulin therapy resulted in sugar control comparable with that published previously [2]. Sugar control in the conventional group improved over the study period. This may be due to the increased awareness of the importance of sugar control. Use of intensive insulin therapy may lead to better sugar control and improved morbidity and mortality in all patients, regardless of the insulin therapy protocol used.

**Table 1**

| | Number of sugars | Mean (SD) (mmol/l) |
|---|---|---|
| Intensive control | | |
| First 3 months | 1300 | 6.7 (2.4)* |
| Second 3 months | 2133 | 6.7 (2.2)* |
| Conventional control | | |
| First 3 months | 1545 | 7.9 (3.0)** |
| Second 3 months | 1936 | 7.2 (1.95)** |

*$P = 0.48$, ** $P = 0.0001$.

**References**
1. Van den Berghe G, Wouters P, Weekers F, *et al.*: *N Engl J Med* 2001, **345:**1359-1367.
2. Krinsley JS: *Mayo Clin Proc* 2004, **79:**992-1000.

## P388

### Tight glycemic control increases the incidence of hypoglycemia in intensive care unit patients

**H Moeniralam[1], P Spronk[2], M Graat[1], M Vroom[1], J Rommes[2], M Schultz[1]**
*[1]Academic Medical Center, Amsterdam, The Netherlands; [2]Gelre Hospital, Apeldoorn, The Netherlands*
*Critical Care* 2005, **9(Suppl 1):**P388 (DOI 10.1186/cc3451)

**Introduction** Hyperglycemia is common in critically ill patients. Tight glycemic control (aimed at blood glucose levels of 4.4–6.1 mmol/l) improved the mortality and morbidity in postoperative intensive care patients [1]. Tight glycemic control, however, bares the risk of hypoglycemia. The present study was performed to investigate whether the introduction of a nurse-driven tight glycemic control protocol in two general ICUs increases the incidence of (severe) hypoglycemia.

**Methods** All measured plasma glucose levels in all patients admitted to a 28-bed academic ICU and to a 10-bed ICU of an affiliated teaching hospital from 1999 to 2003 were retrospectively collected from the hospital information systems. Severe hypoglycemia was defined as blood glucose levels < 2.2 mmol/l, and hypoglycemia as blood glucose levels < 4.4 mmol/l. Comparisons were made between the period before (1999–2001) and after (2002–2003) implementation of tight glycemic control. Directly after analysis of the aforementioned study results, an adjusted tight glucose protocol was implemented in daily ICU practice at the end of 2001.

**Statistics** Data are means ± standard deviation. Comparisons between years were made by chi-square test. Statistical significance was accepted for $P < 0.05$.

**Table 1 (abstract P388)**

**Mean blood glucose values (mmol/l) and percentage of patients developing (severe) hypoglycemia**

| Hospital | 1999 | 2000 | 2001 | 2002 | 2003 |
|---|---|---|---|---|---|
| Mean blood glucose | | | | | |
| AMC | 9.2 ± 3.2 | 9.0 ± 3.2 | 8.8 ± 3.0 | 7.8 ± 2.5* | 7.4 ± 2.5* |
| GH | 9.0 ± 3.6 | 9.2 ± 5.4 | 9.2 ± 4.8 | 8.8 ± 4.1* | 8.5 ± 3.5* |
| % of patients with glucose < 2.2 mmol/l | | | | | |
| AMC | 0.6 | 2.1 | 1.9 | 3.6* | 5.1* |
| GH | 1.4 | 1.0 | 0.7 | 1.6* | 2.2* |
| % of patients with glucose < 4.4 mmol/l | | | | | |
| AMC | 13.4 | 13.1 | 15.8 | 30.0* | 38.8* |
| GH | 12.4 | 12.0 | 11.4 | 17.3* | 17.1* |

* $P < 0.05$ compared with the period before tight glycemic control.

**Results** For all years, > 99% of data were retrieved in both centres. In the AMC approximately 220,000 blood glucose levels were collected (1999–2002: 3869 patients, 2002–2003: 2613 patients); in the GH approximately 35,000 blood glucose levels were collected (1999–2001: 1639 patients, 2002–2003: 1098 patients).

**Conclusions** Tight glycemic control dramatically raises the incidence of hypoglycemia. In parallel the incidence of severe hypoglycemia also increases. Better glucose control regimens are therefore needed to reduce the incidence of hypoglycemia during tight glycemic control.

**Reference**
1. van den Berghe, *et al.*: *N Engl J Med* 2001, **345:**1359-1367.

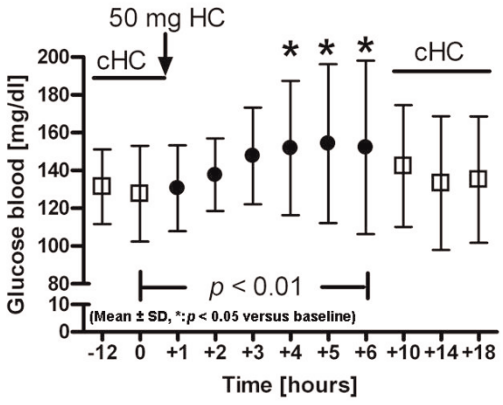
## P389

### Impact of continuous versus bolus low-dose hydrocortisone application on blood glucose in septic shock patients

**S Weber-Carstens, M Deja, F Hokema, A Dimroth, U Kaisers, K Falke, D Keh**
*Charite Hospital, Berlin, Germany*
*Critical Care* 2005, **9(Suppl 1):**P389 (DOI 10.1186/cc3452)

Tight glycemic control in critically ill patients has been shown to reduce ICU and hospital morbidity and mortality [1]. Adjunctive low dose hydrocortisone (HC) therapy in septic shock (200–300 mg/day) might impair tight glycemic control. The degree of metabolic impairment is possibly influenced by the way of HC administration. However, recent Surviving Sepsis Campaign guidelines do not favour either continuous HC administration (cHC) or bolus HC administration (bHC) (4 × 50 mg or 3 × 100 mg) [2]. The purpose of this observational study was to investigate the effects of bHC on blood glucose (Glc) levels in patients with septic shock. The protocol was approved by the local ethics committee. Sixteen patients receiving cHC (200 mg/day) were included. The course of Glc after discontinuing cHC followed by administration of a bolus of 50 mg HC was investigated. Glc values were recorded from charts 12 hours prior to bHC application, straight before bolus application (baseline), and hourly during a 6-hour period. Afterwards, cHC was resumed and Glc measured three times 4 hours apart. Insulin dosage was not adjusted as long as Glc remained <180 mg/dl. Nutritional support was not changed during study period. Mean Glc calculated from all values 12 hours prior to baseline was 131 mg/dl (mean, 95% confidence interval: 121, 142). At baseline, Glc was 128 mg/dl

**Figure 1 (abstract P389)**



(114, 141). Glc increased significantly from baseline until 6 hours ($P < 0.01$, analysis of variance) with peak levels of 154 mg/dl (132, 178) after 5 hours ($P < 0.05$ compared with baseline), and returned to baseline values after 14 hours. The presented data indicate that a bolus of 50 mg HC significantly aggravates impairment of glucose homeostasis. It is conceivable that repetitive HC application three or four times per day would make adequate insulin therapy and glucose monitoring much more time consuming and difficult. In conclusion, although a comparative study on outcome between cHC and bHC does not exist, it seems prudent to administer HC as a continuous infusion in septic shock patients in order to maintain normoglycemia in these patients as tight as possible.

**Reference**

1. van den Berghe, *et al.*: **Intensive insulin therapy in the critically ill patients.** *N Engl J Med* 2001, **345:**1359-1367.
2. Dellinger RP, *et al.*: **Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock.** *Intensive Care Med* 2004, **30:**536-555.

## P390

### Cortisol metabolism in critical illness: effects of intensive insulin therapy

**I Vanhorebeek[1], R Peeters[2], S Vander Perre[1], I Jans[1], P Wouters[1], G Van den Berghe[1]**
*[1]UZ Gasthuisberg, Katholieke Universiteit Leuven, Belgium; [2]Erasmus University Medical Center, Rotterdam, The Netherlands*
*Critical Care* 2005, **9(Suppl 1):**P390 (DOI 10.1186/cc3453)

An appropriate activation of the hypothalamic–pituitary–adrenal axis and cortisol response to critical illness is essential for survival. Indeed, both high and low cortisol levels are associated with increased mortality. We investigated the effect of intensive insulin therapy (IIT), a treatment recently shown to reduce mortality and morbidity of surgical ICU patients [1], on the cortisol response versus conventional insulin therapy (CIT).

All patients included in the large randomized trial [1] who were dependent on intensive care for more than 5 days ($n = 451$) were selected for this study. Serum levels of total cortisol and cortisol-binding globulin (CBG) were measured upon ICU admission, day 5, day 15 and the last day of intensive care. Free cortisol levels were calculated from these data. Baseline characteristics were similar for both patient groups. The two levels of blood glucose control were well maintained throughout the study.

Total cortisol, CBG and free cortisol levels were comparable in both groups on admission to the ICU. On day 5, day 15 and the last day, IIT significantly lowered total cortisol levels. CBG levels were similar except for slightly lower levels in the IIT group on the last day. IIT thus significantly decreased free cortisol on day 5 and day 15. Multivariate logistic regression analysis revealed that reducing cortisol at least in part explained the survival benefit of IIT [1]. Total and free cortisol levels were several-fold higher in critically ill patients receiving exogenous hydrocortisone in so-called 'replacement dose' as compared with patients who did not require such a therapy. IIT appeared to largely exert similar effects in patients with or without hydrocortisone therapy.

In conclusion, by reducing serum cortisol levels, intensive insulin therapy beneficially affected outcome of critically ill patients. Studies are ongoing to elucidate the mechanisms underlying this effect.

**Reference**

1. Van den Berghe, *et al.*: *N Engl J Med* 2001, **345:**1359.

## P391

### Cortisol elimination properties during intermitting hemofiltration in patients with acute renal failure

**V Timokhov[1], I Yakovleva[2]**
*[1]Russian Medical Academy of Postgraduate Edication, Moscow, Russia; [2]Common Reanimatology, RAMS, Moscow, Russia*
*Critical Care* 2005, **9(Suppl 1):**P391 (DOI 10.1186/cc3454)

**Introduction** Application of intermitting hemofiltration (IHF) in treatment of patients with acute renal failure (ARF) has significant stress influence and leads to elimination of essential amounts of cortisol and other adaptive hormones.

**Materials** Nineteen patients (11 males/eight females) 11–62 years of age with ARF were examined. Forty-six IHF procedures were performed with the mean duration 6.5 ± 0.6 hours; filtration volume 50.2 ± 2.6 (18–85) l; index 1.03 ± 0.8 (0.45–1.53). The filtration rate was 128 ± 9 (27–260) ml/min. The cortisol concentration in the plasma and the filtrate was measured by radioimmune assay.

**Results** The cortisol content in the plasma of controls ($n = 32$) was 334 ± 20 nM/l. At the beginning of the IHF procedures the cortisol concentration in plasma of patients with ARF was 672 ± 83 nM/l ($n = 36$; $P < 0.001$). At the end of the procedures the mean plasma cortisol concentration increased to 1197 ± 199 nM/l ($P < 0.001$). Cortisol concentrations in the effluent were 8303 ± 543, 7993 ± 532 and 8414 ± 416 nM/l at the beginning of the procedure, at the end and in total effluent volume accordingly.

**Conclusion** The phenomenon of cortisol 'hyperfiltration' revealed in this study may be explained by filtration of significant amounts of this hormone from the surface of erythrocytes that need to be investigated further.

## P392

### Effect of a single dose of etomidate on adrenal function in patients with trauma

**K Price, U Allen, G Mandersloot, P Shirley, D McAuley**
*Royal London Hospital, London, UK*
*Critical Care* 2005, **9(Suppl 1):**P392 (DOI 10.1186/cc3455)

Studies investigating the relationship between adrenal insufficiency in sepsis and the potential need for steroids have been complicated by the use of etomidate, an anaesthetic agent that has been shown to cause adrenal impairment. Controversy still exists regarding the effects of a single dose of etomidate on adrenal function and a temporal or dose-dependent effect may occur. In an attempt to remove the confounding effect of sepsis on adrenal function, we studied a group of severely injured trauma patients to determine whether a single dose of etomidate effects adrenal function.

Trauma patients admitted to the intensive care unit of the Royal London Hospital who had received etomidate as their induction agent were enrolled within 36 hours of admission. Patients received varying doses of etomidate on induction. Plasma cortisol was measured at baseline and 60 min following a short ACTH stimulation test (250 μg synthetic ACTH). Responders were defined as having an increment in cortisol of > 250 nmol/l. Data were analysed using an unpaired *t* test or chi-square test as appropriate.

Twenty-two patients (17 male) with polytrauma were recruited. Nine patients had impaired adrenal function. Overall, compared with responders, there was no difference between dose of etomidate received or time from induction (Table 1).

There was no difference in incidence of adrenal impairment in those patients who had their adrenal function assessed pre or post 18 hours from receiving etomidate.

In conclusion, patients with severe polytrauma who have received etomidate commonly have adrenal impairment. The clinical significance of these findings is unclear but it is not possible to exclude an inhibitory effect of etomidate on adrenal function. Prior to commencing steroids in the critically ill with adrenal insufficiency, it is important to consider whether patients have received etomidate.

**Table 1 (abstract P392)**

| | Non-responders | Responders |
|---|---|---|
| *n* | 9 | 13 |
| Etomidate dose (mg) | 15 (4) | 15 (4) |
| Time to test (hours) | 17 (9) | 21 (6) |

## P393

### Influence of hydrocortisone on platelet receptor expression and aggregation *in vitro*

**T Schuerholz[1], O Keil[2], M Vonnemann[2], L Friedrich[2], G Marx[1], D Scheinichen[2]**
*[1]Friedrich-Schiller-University, Jena, Germany; [2]Medical School, Hannover, Germany*
*Critical Care* 2005, **9(Suppl 1):**P393 (DOI 10.1186/cc3456)

**Introduction** Hydrocortisone differentially modulates inflammatory mediators and expression of adhesion molecules. Previously, a randomised controlled trial showed that hydrocortisone attenuates cell interactions in septic shock [1]. However, the effect of 'low'-dose hydrocortisone treatment on platelet activation has not yet been evaluated systematically.
**Objective** To evaluate the influence of hydrocortisone levels on platelet activation *in vitro*.
**Methods** Citrated blood samples were drawn from healthy blood donors ($n = 25$, 36% male, age: 40 ± 10 [mean ± standard deviation]). Exclusion criteria were smoking, diabetes mellitus, diseases and drugs interfering with cortisone levels or platelets. After measuring the morning cortisol level, blood samples were adjusted with hydrocortisone (Pharmacia, Erlangen, Germany) to final concentrations of 4.5 μg/ml (group 1), 9 μg/ml (group 2, low dose) and 90 μg/ml (group 3), respectively. The control group received no additional hydrocortisone. Samples were incubated for 10 min at 37°C with fluorescence-labeled monoclonal antibodies against CD62P, CD41, CD45, CD42b (all: Beckman-Coulter, Krefeld, Germany) or PAC-1 (Becton Dickinson, San Jose, CA, USA). To evaluate platelet reactivity 5 μM thrombin-receptor-agonist-peptide-6 (TRAP-6; Bachem, Germany) or 2.5 μM adenosine-di-phosphate (ADP; Sigma, Germany) were added. Analyses were performed in a flow cytometer. The mean fluorescence intensity (MFI) and percentage of $CD45/41^+$ complexes was calculated. Determination of platelet aggregation was performed by turbidimetric procedure (BCT; Dade Behring, Marburg, Germany). Aggregation was induced with ADP (200 μM/l; Dade Behring), collagen (2 mg/l; Dade Behring) and epinephrine (100 μM/l; Dade Behring). Intergroup differences were compared by one-way analysis of variance.
**Results** The initial cortisol level was 11.6 ± 3.5 μg/dl. Hydrocortisone administration had no significant influence on expression of PAC-1, CD62P and $CD45/41^+$ complexes, with and without stimulation. In contrast, we observed a significant lower expression of CD42b in group 3 compared with the control group only without activation ($P = 0.047$). A similar observation was made for CD41 expression (group 3 vs control: unstimulated: $P = 0.035$). Differences between the control and groups 1 and 2 were not significant with either activator. Aggregometry showed significant later onset of maximum aggregation after activation with ADP and collagen (group 3 vs control: collagen: $P = 0.001$; ADP: $P = 0.048$).
**Conclusion** This *in vitro* study demonstrates that administration of low-dose hydrocortisone neither reduces expression of investigated platelet receptors nor attenuates begin of maximum aggregation in doses recommended in septic shock. We therefore conclude that 'low'-dose hydrocortisone might not result in impaired platelet function.

**Reference**

1. Keh D, *et al.*: *Am J Respir Crit Care Med* 2003, **167:**512-520.

## P394

### Outcome of septic shock patients with relative adrenal insufficiency

**G Friedman[1], R da Silva[2], M Becker[2], L Gehrke[2]**
*[1]Hospital de Clinicas, Porto Alegre, Brazil; [2]Complexo Hospitalar Santa Casa, Porto Alegre, Brazil*
*Critical Care* 2005, **9(Suppl 1):**P394 (DOI 10.1186/cc3457)

**Introduction** Septic shock may be associated with relative adrenal insufficiency. A replacement therapy with low doses of corticosteroids has been proposed to treat septic shock.
**Objective** To describe the outcome of a cohort of septic shock patients with a treatment strategy guided by a short corticotropin test.
**Design and setting** An observational and prospective cohort of severe septic shock patients treated in a general ICU of a university hospital.
**Materials and methods** Thirty-three patients who fulfilled criteria for severe septic shock. In all patients a short corticotropin test (250 μg) with cortisol measured at 0, 30 and 60 min was performed. The response to the test was considered whenever the difference between baseline cortisol and pick cortisol was greater than 9 mg/dl. Low-dose corticosteroids (hydrocortisone 50 mg, intravenously, 6/6 hours) was given to all patients and maintained only when the patient was a non-responder.
**Main outcome measure** Twenty-eight-day mortality.
**Results** The total mortality rate was 65% (21/32). The non-survivors where older (68.5 ± 11.5 vs 53.9 ± 20.2, $P = 0.014$), and had a higher baseline cortisol (27.5 ± 17.7 vs 17.0 ± 12.9 μg/dl, $P = 0.043$). APACHE II score, pick cortisol, delta cortisol and albumin where not different. There were 15 responders and 17 non-responders to the corticotropin test. In non-responders, the mortality rate was 64% (11/17) and in responders it was 66% (10/15). Responders had a higher baseline cortisol (29.1 ± 20.7 vs 19.2 ± 11.1 mg/dl, $P$ = not significant), higher pick cortisol (45.4 ± 21.9 vs 23.7 ± 10.3 μg/dl, $P = 0.001$) and higher delta cortisol (16.3 ± 5.9 vs 4.7 ± 2.3 μg/dl, $P < 0.001$). Age, APACHE II score and albumin were similar. Vasopressor therapy was withdrawn in 20 patients and eight patients were responders (40%). Among 12 patients not weaned from vasopressors, seven (58%) were responders. Hypoalbuminemic (albumin < 2.5 g/dl) and non-hypoalbuminemic patients had no differences among measured variables. However, 60% (15/25) of hypoalbuminemic but only 28% (2/7) of normoalbuminemic patients were non-responders.
**Conclusions** Mortality rates among responders and non-responders were equivalent and may indicate a beneficial effect of low-dose hydrocortisone. Hypoalbuminemia may influence the response to the corticotropin test once most hypoalbuminemic patients were non-responders.

**P395**

## Low-dose and high-dose corticotropin stimulation test in septic shock patients

**J Schweitzer, C Broux, J Brun, P Lavagne, J Payen, C Jacquot**
*Grenoble Hospital, Grenoble, France*
*Critical Care* 2005, **9(Suppl 1):**P395 (DOI 10.1186/cc3458)

**Introduction** Septic shock is frequently associated with relative adrenal insufficiency (RAI). RAI increases mortality and hydrocortisone supplementation improves survival in septic shock patients. There is no consensus about RAI diagnosis criteria. With the standard corticotropin stimulation test (SCST) (250 μg) ACTH levels reaches 100 times the physiological concentration. A low-dose corticotropin stimulation test (LDCST) (1 μg) is closer to physiological ACTH levels.
**Objective** To determine whether a LDCST (1 μg) can reveal RAI in septic shock patients when the SCST (250 μg) does not diagnose RAI.
**Methods** A prospective cohort study conducted between October 2003 and May 2004 in an adult intensive care unit of a teaching hospital in France. A baseline cortisol concentration was obtained in septic shock patients. An intravenous injection of 1 μg corticotropin (LDCST) followed 90 min later by an injection of 249 μg corticotropin (SCST) was performed. Cortisol concentrations were obtained 30 and 60 min after each test. All patients received hydrocortisone (50 mg/6 hours intravenous bolus) and fludrocortisone (50 μg tablet once daily) while awaiting the results of cortisol assesment. Patients were considered without RAI if Delta max $>$ 9 mg/dl. Delta max is defined as the difference between T0 and the highest value between T30 and T60 of each test. Hydrocortisone and fludrocortisone were delivered for 7 days if the patient had RAI on SCST and stopped in the other cases.
**Results** Twenty-three patients with septic shock were enrolled. Their mean age was 60 ± 14 years; 16 were male. IGS II was 52 ± 21 and the SOFA score at admission was 9 ± 3. Sixteen patients (63%) were admitted for nosocomial infection, 14 (61%) for peritonitis, six (26%) for pulmonary infection and three for other sites of infection. Seven patients died at day 28 (33%) and nine in the intensive care unit (40%). Baseline cortisol levels were 12.69 ± 7.24 μg/dl. Twenty-one patients met the diagnosis criteria of RAI with the LDCST and 18 with the SCST (Delta max LDCST: 10.78 ± 1.37; Delta max SCST: 17.44 ± 4.53). Three patients had RAI with the LDCST but not with the SCST.
**Conclusion** The incidence of RAI was very high in our study population with the SCST (78%). We found three patients without RAI according to the SCST but showing impaired response to the LDCST. The small number of patients in this situation does not allow any conclusion about the best test to choose. It seems of interest to enlarge our cohort of patients to draw clinically relevant information.

**P396**

## Sepsis-related adrenal dysfunction in HIV-positive and negative critically ill patients using a 1 μg short synacthen test

**S Omar, P Ferrao, S Caroline, L Mathivha, S Rajah**
*University of Witwatersrand, Johannesburg, South Africa*
*Critical Care* 2005, **9(Suppl 1):**P396 (DOI 10.1186/cc3459)

**Introduction** Sepsis is a common problem in our ICU, often leading to hypotension requiring vasopressor support. Adrenal dysfunction is thought to be common in septic patients. HIV-related opportunistic infections are known to be the most common cause of adrenal dysfunction. The prevalence of HIV in the community we service is around 20%. We will present here the preliminary results from a study on septic patients admitted to our ICU. We have assessed HIV status and CD4 counts on consecutive ICU admissions over a 4-month period All patients requiring vasopressors have undergone a synacthen test.
**Method** A prospective, observational, experimental study at an academic ICU. A presenting sample was taken over a 4-month period. Ethics approval was obtained from the University Ethics Committee.
**Testing** A 1 μg low-dose short synacthen test (SST). Baseline bloods for renin, aldosterone, HIV and CD4. The laboratory was blinded to patient details and the physician blinded to results. One hundred and twenty-six patients enrolled and 40 synacthen tests were carried out. Results were available for 68 patients and 20 synacthen tests as of 14 December 2004. No renin, aldosterone and CD4 counts were available at submission of abstract.
**Results** Sixty-eight patients admitted to the ICU were enrolled and followed up to D28 in 6 weeks. Twenty SSTs were performed for refractory hypotension within 24 hours of initiating vasopressors. The incidence of adrenal dysfunction (AD) was highest with a stress cortisol (SC) $<$ 690 nmol/l or a delta cortisol (D30/60) $<$ 250 nmol/l (89% in either case). Primary AD was more common then secondary AD and tertiary AD combined (89% vs 11%). A SC $<$ 690 or a (D30/60) $<$ 250 during a SST were more sensitive than a SC of $<$ 550 nmol/l in detecting AD (89% vs 74%). Hemodynamic response (HR) is defined as an increase in MAP or decrease in vasopressor requirements in the 24 hours post steroid initiation. At a threshold of 10%, 68% responded to steroid treatment. The median increase in MAP or vasopressor decrease during the 24 hours post steroid initiation was 28%. There was no significant difference in mortality between steroid-treated AD and patients without AD ($P = 0.91$). Of the 68 patients, 17 were HIV-positive and 51 were HIV-negative. The period prevalence (1.5 months) is 25%. There was no significant difference in mortality between HIV-negative and HIV-positive (without AIDS-defining illnesses) patients ($P = 0.29$).
**Conclusion** There is a high incidence of AD in septic shock. The most sensitive means of detection is a SC $<$ 690 nmol/l or a D30/60 $<$ 250 nmol/l. Primary AD is much more common than secondary AD. The increased mortality and haemodynamic instability of AD is eliminated by steroid treatment. Finally, HIV status alone does not impact on mortality in disease unrelated to HIV/AIDS. On completion we will be able to comment on the diagnostic performance of renin and aldosterone and their relationship to AD and ARF and the CD4 count, and its ability to predict mortality in HIV-positive patients

**P397**

## The time course of adrenocortical hormones and cytokines in sepsis and/or septic shock

**I Dimopoulou, S Tsagarakis, M Zervou, E Douka, S Orfanos, A Kotanidou, O Livaditi, C Augustatou, M Tzanella, N Thalassinos, A Armaganidis, C Roussos**
*University of Athens Medical School, Athens, Greece*
*Critical Care* 2005, **9(Suppl 1):**P397 (DOI 10.1186/cc3460)

The present study was carried out to evaluate the time course of serum adrenocortical hormones and cytokines in critically ill patients with sepsis and/or septic shock. To this end, 56 patients (42 men) with a median age of 53 years (range 17–82 years) were investigated. At study entry, the mean APACHE score was 20 and the median SOFA score was 11. Blood was drawn to measure cortisol, corticotropin (ACTH), dehydroepiandrosterone-sulphate (DHEAS), IL-6 and tumor necrosis factor alpha (TNF-α) levels

within 48 hours of the onset of sepsis and/or septic shock, and thereafter every second day for 14 days, or until death or ICU discharge. Median cortisol and DHEAS run in parallel and remained unchanged during the study period (17, 18, 17, 14, 17 and 18 μg/dl, $P = 0.42$, 1.188, 1.145, 1.190, 1.220 and 873; 1.202 ng/ml, $P = 0.97$, respectively). Median ACTH increased significantly during the entire observation period (21, 24, 28, 34, 32 and 43 pg/ml, $P = 0.008$). TNF-α levels were high and decreased gradually (2, 2, 1, 0, 0 and 0 pg/ml, $P < 0.001$). IL-6 concentrations were high initially, but decreased abruptly during the first week; thereafter, they reached a plateau (344, 215, 169, 118, 128 and 93 pg/ml, $P < 0.001$).

In conclusion, during the course of sepsis and/or septic shock, serum glucocorticoids and adrenal androgens do not change. During the first week, the hypothalamic–pituitary–adrenal axis is activated by both ACTH and IL-6; the axis is subsequently stimulated primarily by ACTH.

## P398

### Adrenal insufficiency in septic shock: what should one do at the present time?

**J Sales, S Lima, P Souza**

*[1]Hospital de Clínicas Niterói, Brazil; [2]Hospital da VOT Penitência, Rio de Janeiro, Brazil*

*Critical Care* 2005, **9(Suppl 1):**P398 (DOI 10.1186/cc3461)

**Introduction** In the past years many studies have demonstrated the occurrence of relative adrenal insufficiency and immunologic and hemodynamic effects of low-dose hydrocortisone in septic shock. Despite this evidence, the optimal approach to ensure the diagnoses is not yet clear.

**Methods** We conducted a prospective cohort study in two ICUs from March 2003 to March 2004. The patients who developed septic shock and were under mechanical ventilation had their serum cortisol measured. The diagnoses of septic shock were made in accordance with the criteria proposed by ACCP/SCCM. The hydrocortisone was administrated every 6 hours (200 mg intravenously daily) during 7 days or less, according to the hemodynamic response and the relationship with the serum cortisol level (≤ 25 μg/dl). Two criteria were used to make the diagnoses: serum cortisol level ≤ 25 μg/dl and the weaning of vasoative drugs in the first 24 hours or dose reduction in at least 50%. The APACHE II score and SOFA score were used to evaluate the seriousness.

**Results** Fifty-nine patients were evaluated. Average age was 69 years, 30 (50.8%) were male. The average APACHE II score was 24 and the SOFA score on the first day was 10.5. The average plasma cortisol was 27.5 μg/dl (4–114). Cortisol ≤ 25 μg/dl was identified in 30 (50.8%) patients. The weaning from vasoative drugs or the dose reduction in at least 50% was observed in 25 patients. The sensitivity of a baseline cortisol ≤ 25 μg/dl associated with hemodynamic response to predict adrenal insufficiency was 83.3% (95% confidence interval; 72.5–94). According to this criterion, relative adrenal insufiency was diagnosed in 33.8% in this group.

**Conclusion** Adrenal insufiency appears to be common in septic shock patients. Hemodynamic response to hydrocortisone linked to a serum cortisol ≤ 25 μg/dl seems to be a good way to make the diagnosis. Until we have the best cut-off value of serum cortisol and a definitive response about the validity of the corticotropin test in septic patients, the clinical response to corticosteroids should be taken into consideration to make that diagnosis.

## P399

### Adrenal failure in neurological and septic critically ill patients

**D Salgado[1], R Paiva[1], M Rodrigues[1], J Rocco[2], J Verdeal[1]**

*[1]Hospital Barra D'or, Rio de Janeiro, Brazil; [2]Hospital Universitario Clementino Fraga Filho, Rio de Janeiro, Brazil*

*Critical Care* 2005, **9(Suppl 1):**P399 (DOI 10.1186/cc3462)

**Introduction** Adrenal failure (AF) is known to develop during the course of sepsis and to adversely affect the prognosis of the patients. Neurological critically ill patients may additionally be susceptible to development of AF due to disruption of the hypotalamic–pituitary–adrenal axis.

**Objectives** To determine the response to the corticotropin stimulation test with low dose (1 μg) and high dose (249 μg) in septic patients and to compare the frequency of AF in the neurological and non-neurological subsets.

**Materials and methods** Patients admitted to an ICU from May 2002 to November 2004, with septic shock, additionally registered whether they had associated neurological diseases (head trauma, acute cerebrovascular disorders, postoperative) or not, were submitted to the corticotropin stimulation test. A baseline cortisol level was first obtained, then patients received an intravenous injection of 1 μg corticotropin (low dose) followed 60 min later by an injection of 249 μg (high dose). The cortisol level was obtained 60 min after low-dose and high-dose corticotropin. The difference between the higher and baseline cortisol level was registered as Δmax. We defined AF when the baseline cortisol level was lower than 25 μg/dl or Δmax was lower than or equal to 9 μg/dl. The EPiINFO version was used for data analysis, and $P < 0.05$ was considered significant.

**Results** Eighty-two patients were enrolled, 47 were female. The mean age was 71. The overall rate of baseline cortisol level lower than 25 μg/dl was 79.3% (65/82) and Δmax lower than or equal to 9 μg/dl was 19.5% (16/82). The cortisol levels were significantly higher in the neurological group than in the non-neurological group, as presented in Table 1. The frequency of cortisol level lower than 25 μg/dl was similar in the neurological and non-neurological disease groups (33/43 vs 32/39 – odds ratio 1.37 [95% confidence interval, 0.41–4.83]), but the frequency of Δmax < 9 μg/dl was higher in the neurological patients (9/39 vs 7/43), although non-statistically significant ($P = 0.2$).

**Conclusion** Patients with septic and neurological diseases have higher baseline and post-corticotropin cortisol levels than non-neurological patients, but the frequency of AF is similar between both groups.

**Table 1 (abstract P399)**

| | *n* | Baseline cortisol (μg/dl) | Low-dose cortisol (μg/dl) | High-dose cortisol (μg/dl) | Δmax (μg/dl) |
|---|---|---|---|---|---|
| Neurological disease | 39 | 21.6 ± 13.1 | 37.5 ± 16.9 | 49.2 ± 21 | 27.5 ± 17.9 |
| Non-neurological disease | 43 | 15 ± 8.6 | 25.2 ± 10.7 | 33.7 ± 13.5 | 18.6 ± 11 |
| | Not significant | $P = 0.006$ | $P = 0.0006$ | $P = 0.001$ | $P = 0.03$ |

**P400**

## Relative adrenal insufficiency in critically ill hematology patients

**J Cerman, M Cermanova, R Mottl, L Sobotka, J Maly**
*Faculty Hospital, Hradec Kralove, Czech Republic*
*Critical Care* 2005, **9(Suppl 1):**P400 (DOI 10.1186/cc3463)

**Aim** Sepsis is the most common cause of death of hematology patients in intensive care units. The adrenal gland is potentially involved in sepsis. Impaired functions of the adrenal gland can be caused by hemorrhage, tumor infiltration, drugs and suppression after glucocorticoid treatment. The goal of the study was to evaluate adrenal functions in a group of critically ill hematology patients.
**Patients and methods** Forty critically ill patients with hematological disease, mean age 57 ± 14 years, 22 of them women. Mortality was 48%. The mean APACHE II score was 37 (22–48). We performed a 250 μg short intravenous corticotropin test and we determined plasma concentrations of cortisol before and 30 and 60 min after the test. According to the results patients were classified as having adrenal insufficiency or not.
**Results** The incidence of the adrenal insufficiency depends on the criteria used. Using a basal cortisol level lower than 414 nmol/l (15 mg/dl), the incidence of adrenal insufficiency was 27.5% (11 patients). Using a basal cortisol level or cortisol response to corticotropin lower than 250 nmol/l, the incidence of adrenal insufficiency was 60% (20 patients). When we use both these criteria, the incidence of adrenal insuficiency was 12.5% (five patients) and all these patients died. Patients with adrenal insufficiency had higher mortality.
**Conclusion** There is a high incidence of adrenal insufficiency in critical ill hematology patients. These patients should undergo evaluation of adrenal functions to reveal patients with a need of hydrocortisone treatment.

**P401**

## The relative adrenal insufficiency syndrome in the intensive care unit: incidence and relationship to outcome

**I Dimopoulou, K Stamoulis, P Lyberopoulos, E Douka, P Alevizopoulou, A Armaganidis, N Thalassinos, S Tsagarakis**
*University of Athens Medical School, Athens, Greece*
*Critical Care* 2005, **9(Suppl 1):**P401 (DOI 10.1186/cc3464)

The aim of the current study was to investigate the incidence of relative adrenal insufficiency in a large cohort of critically ill patients. Furthermore, we wished to assess the relationship of adrenal function tests to outcome of patients admitted to an adult medical and surgical ICU.
To this end, 151 (119 men) critically ill patients having various principal diagnoses were studied. The median age was 52 years (range 17–84 years). The median APACHE II score was 11. Blood was sampled within 48 hours of admission for measurement of serum concentrations of baseline cortisol and corticotropin (ACTH). Immediately after, a low-dose (1 μg) ACTH stimulation test was performed. Patients having stimulated cortisol levels below 18 μg/dl were defined as non-responders to the test.
Median values for baseline cortisol and ACTH were 16.0 μg/dl (range 0.3–61.3 μg/dl) and 16.8 pg/ml (range 0.9–166.4 pg/ml) respectively. The median stimulated cortisol value was 22.4 μg/dl (range 4.7–70.0 μg/dl) and the median increment in cortisol was 7.1 μg/dl (range 0.2–25.6 μg/dl). There was a positive correlation between ACTH and baseline cortisol ($r = 0.42$, $P < 0.001$). Thirty-nine (26%) patients were non-responders to the low-dose ACTH stimulation test. Overall mortality was 26%. Non-survivors were older (64 vs 24 years, $P = 0.002$), and had a higher APACHE II score (13 vs 11, $P = 0.007$) compared with survivors. There were no differences between the two groups with regard to baseline or stimulated cortisol levels. Similarly, ACTH and the increment in cortisol was comparable in the two groups.
In conclusion, this study involving a large number of severely ill patients showed that the relative adrenal insufficiency syndrome is quite common in the ICU; however, baseline or stimulated cortisol concentrations do not differ between survivors and non-survivors on admission to the ICU.

**P402**

## Incidence of adrenal insufficiency within 10 days of traumatic brain injury

**F Bernard, J Outtrim, D Menon, B Matta**
*Addenbrooke's NHS Trust, Cambridge, UK*
*Critical Care* 2005, **9(Suppl 1):**P402 (DOI 10.1186/cc3465)

Adrenal insufficiency (AI) is common in septic shock, and the physiologic replacement of hydrocortisone improves outcome [1]. Head injury (HI) has been shown to cause AI in the subacute phase (>10 days) with a reported incidence of approximately 15% [2,3], but there are no data on early AI, at times when it is most likely to influence ICU management. Furthermore, analysis of available data is confounded by variations in the definition of AI [4,5]. We aim to describe adrenal function in the first 10 days after injury using various suggested definitions of AI in critical care [4,5].
We retrospectively analysed patients who had a stimulation test performed within 10 days of admission to our neurointensive care unit. Tetracosactide (Synacthen) was administered as a 250 μg bolus and cortisol levels measured at 0, 30 and 60 min. AI was defined as a baseline cortisol level below 414 mmol/l and failure to rise by 250 mmol/l after Synacthen administration. All patients who showed AI or responded clinically to a trial of steroid therapy received 200–400 mg hydrocortisone per day while on vasopressor therapy.
One hundred and thirteen patients were analysed. Mean age was 35 ± 15 and 79% were male. Four percent, 25% and 70% had mild, moderate and severe HI defined by the GCS on admission. Mean APACHE II and ISS scores were 15 ± 6 and 24 ± 10. The incidence of AI according to baseline cortisol level was 78%. The cortisol level failed to rise in 48% and 27% of patients at time 30 and 60 min, respectively. Primary adrenal insufficiency defined by both low baseline cortisol and failure to react to synacthen was present in 28% and 13% of patients at time 30 and 60 min. All patients had baseline cortisol levels below 690 mmol/l. Cortisol remained below 500 mmol/l after stimulation in 49% and 22% of patients at 30 and 60 min. The incidence of AI, using any of the definitions in the literature, was unrelated to APACHE II or ISS score or GCS on admission, or to ICU length of stay or outcome (defined using the Glasgow Outcome Score).
A 60-min sampling time point may be more appropriate to evaluate the response to Synacthen stimulation. During the first 10 days after HI, secondary AI was present in 78% of patients and primary AI in at least 15%. These incidences might be higher if less stringent definitions are used. Injury and/or illness severity indices do not predict AI. While AI was not predictive of outcome in this study, all subjects with AI received steroid replacement. Such a high incidence of AI may have major therapeutic implications.

**References**

1. Annane D: *JAMA* 2002, **288:**862.
2. Dimopoulou I: *Crit Care Med* 2004, **30:**1216.
3. Dimopoulou I: *Intensive Care Med* 2004, **32:**404.
4. Cooper MS: *N Engl J Med* 2003, **348:**727.
5. Marik PE: *Chest* 2002, **122:**1784.

## P403

### Endocrine responses to major abdominal surgery

**I Dimopoulou, E Douka, I Mavrou, P Kopterides, M Lignos, P Lyberopoulos, C Augustatou, M Tzanella, S Orfanos, A Macheras, G Kostopanagiotou, P Trivizas, E Potoula, N Thalassinos, S Tsagarakis, A Armaganidis**
*University of Athens Medical School, Athens, Greece*
*Critical Care* 2005, **9(Suppl 1):**P403 (DOI 10.1186/cc3466)

The purpose of the current study was to assess the pattern of endocrine responses in patients undergoing elective major abdominal surgery. To this end, 16 patients (nine women) with a mean age of 71 ± 9 years (range, 48–87 years) were studied. Underlying diagnoses included carcinoma of the pancreas ($n = 5$), stomach ($n = 4$), colon ($n = 4$) and rectum ($n = 3$). Blood was taken before surgery (day –1), immediately after the operation (day 0), and on the two subsequent days (day 1 and day 2). At each sample time cortisol (F), corticotropin (ACTH), triiodothyronine (T3), free thyroxine (fT4), thyroid-stimulating hormone (TSH), and insulin-like growth factor 1 (IGF-1) were determined. Serial measurements were analyzed by one-way analysis of variance followed by Dunn's test for multiple comparisons, and the results are presented in Table 1 (median values or mean ± standard deviation).

**Table 1**

| | Day –1 | Day 0 | Day 1 | Day 2 | *P* value |
|---|---|---|---|---|---|
| F (μg/dl) | 15 | 20 | 17 | 13 | 0.03 |
| ACTH (pg/ml) | 21 | 129 | 10 | 8 | 0.001 |
| T3 (ng/dl) | 100 ± 22 | 82 ± 18 | 72 ± 17 | 69 ± 15 | 0.001 |
| fT4 (ng/dl) | 1.3 ± 0.2 | 1.5 ± 0.3 | 1.4 ± 0.3 | 1.4 ± 0.3 | NS |
| TSH (μIU/ml) | 1.0 | 1.1 | 0.9 | 1.0 | NS |
| IGF-1 (ng/ml) | 75 | 46 | 58 | 49 | 0.001 |

NS, not significant.

In conclusion, major surgical stress results in a profound, albeit transient, activation of the hypothalamic–pituitary–adrenal axis. Furthermore, surgery leads to a suppression of thyroid and somatotroph function, and this effect persists for more than 2 days. The relationship between hormonal responses and patients' outcome remains to be determined.

## P404

### Acute rhabdomyolysis in the intensive care unit

**M Pedonomos, M Tsirantonaki, G Psoma, C Mandila, G Koukoulitsios, N Katsarelis, H Angelopoulou, G Stathopoulos, N Noulas, S Phousphoukas, G Theodoropoulos, A Karabinis**
*General Hospital, Athens, Greece*
*Critical Care* 2005, **9(Suppl 1):**P404 (DOI 10.1186/cc3467)

**Introduction** The aim of this clinical trial is to examine the factors that influence prognosis of acute rhabdomyolysis (ARM) in critically ill ICU patients.
**Methods** We studied retrospectively 39 ICU patients with ARM. Mean age: 47.8 ± 24.5 years, mean stay: 20.3 ± 11.5 days. Underlying diseases: multiple trauma 26, complicated surgery 9, status epilepticus 2, drug poisoning 2. All patients underwent mechanical ventilation. Laboratory data included initial and peak values, as well as frequent measurements at least twice a day, of: serum creatinine (CR), creatine phoshokinase (CPK), blood urea nitrogen (BUN), potassium, sodium, calcium, magnesium, phosphate, white blood cell count (WBC), hematocrit (HT), transaminases, bilirubin, lactate dehydrogenase (LDH), and myoglobulin of urine and urine toxicology screen.
**Results** Intensive therapy began very early upon diagnosis with intravenous administration of fluids, furosemide and/or mannitol and bicarbonates besides etiological treatment, where was possible. The initial value of CR was normal (≤ 1.3mg%) in 22 patients (56.4%). The mean percentage decrease in HT was 13.1 ± 2.8% after 24 hours of hydration (showing approximately the percentage of initial volume depletion). In 11 patients (28.2%) CPK was >10,000 IU/l and in five patients (12.8%) > 20,000 IU/l. BUN ≤ 50 mg% was initially found in 20 patients (51.3%) and WBC <11,000/mm$^3$ in 19 (48.7%). The urine pH (measured every 3–6 hours) had a value < 6.0 in two patients (5.1%), while 23 (59.0%) developed acute renal failure (ARF) and required hemodialysis. Mortality rates: 8/39 (20.5%).
**Conclusion** (1) Normal initial CR, initial BUN < 50 mg%, initial WBC <11,000/mm$^3$ and less than 15% decrease of HT (volume depletion) were associated with either normal renal function or a slight ARF not requiring hemodialysis ($P < 0.05$). (2) An elevated initial value of CPK >10,000 IU/l was associated with ARF requiring hemodialysis ($P < 0.01$) [1], longer duration of mechanical ventilation ($P < 0.05$), longer ICU stay ($P < 0.05$) and higher mortality rates (< 0.05). (3) Contrarily, high values of urine myoglobulin were not associated with severe ARF or elevated mortality rates ($P < 0.1$).

**Reference**

1. de Meijer AR, Fikkers BG, de Keijzer MH, van Engelen BG, Drenth JP: **Serum creatine kinase as predictor of clinical course in rhabdomyolysis: a 5-year intensive care survey.** *Intensive Care Med* 2003, **29:**1121-1125.

## P405

### Early definitive stabilization versus damage control orthopaedics for femur shaft fractures in the multiply injured patient

**S Morgan[1], M Tuttle[1], W Smith[1], C Hartshorn[2], D Ciesla[1], A Williams[1], E Moore[1]**
*[1]Denver Health Medical Center, Denver, CO, USA; [2]University of Colorado, Denver, CO, USA*
*Critical Care* 2005, **9(Suppl 1):**P405 (DOI 10.1186/cc3468)

**Background** The optimal timing and treatment of patients with femoral shaft fractures and associated head, thoracic, or abdominal injury remains controversial. This study examines the acute patient outcomes associated with the evolution of early total care to damage control orthopaedics for multiply injured patients with femoral shaft fractures.
**Methods** This study was a retrospective comparison of two sequential protocols for the care of multiply injured patients with femoral shaft fractures. From 1993 to 1998 our institutional protocol for these patients consisted of early total care (ETC) with intramuscular nailing or femoral traction within 24 hours. From 1998 to 2003 we placed femoral external fixation on all polytrauma patients meeting specific injury criteria. Study inclusion criteria included severely injured skeletally mature patients (closed physes) with femoral shaft fractures. Patients were determined to be severely injured if they presented with an ISS ≥ 25, AIS of the head ≥ 3, or hypotension. All included patients received fracture stabilization within 24 hours of presentation. The cohort population was compared with respect to age, sex, and ISS. Primary outcome measures for comparison between these groups included mortality, pulmonary complications (ARDS score), and multiple organ failure (MOF score). The groups were also compared regarding operative time, ICU length of stay, and hospital length of stay.

**Results** During the ETC treatment period 102 patients with femur shaft fractures were identified, 27 of which met the inclusion criteria. During the DCO period 202 patients were identified, 38 of which met the inclusion criteria. The patient groups were comparable regarding age, gender, and injury severity score. There was no difference between the groups in terms of ARDS incidence, lung scores, MOF incidence, MOF score, ICU LOS, or hospital LOS. The DCO group had a significantly shorter OR time.
**Conclusion** In our experience the method of fracture fixation (DCO vs ETC) did not appear to impact the incidence of systemic complications (ARDS and MOF) in the polytrauma patient with an associated femoral shaft fracture. However, we feel that multidisciplinary care is facilitated with DCO and that the decreased initial operative exposure appears to benefit specific subsets of patients. The debate over the optimal timing and method of femur fixation will continue until a treatment protocol can be validated based on a high-quality study with a large number of patients. This study provides the basis for a prospective, randomized, multicenter trail of DCO versus ETC for femur shaft fractures in multiply injured patients.

## P406

## The efficacy of HPLC for the diagnosis of 'illegal drug' intoxication

**J Yuzawa, T Suzuki, M Ishikawa, M Takeda, N Sasaki, A Yaguchi**
*Tokyo Women's Medical University, Tokyo, Japan*
*Critical Care* 2005, **9(Suppl 1):**P406 (DOI 10.1186/cc3469)

Intoxicated patients are not uncommonly admitted to the emergency room (ER) due to unconsciousness. In Japan, 'illegal drug' abuse has increased recently among young people. Diagnosis of 'illegal drug' intoxication is often limited to information from patients or surroundings. The purpose of this study was to evaluate the efficacy of HPLC for the diagnosis of 'illegal drug' intoxication. The clinical records from six patients with 'illegal drug' intoxication who were admitted to our ER between 2000 and 2004 were reviewed. The HPLC system was performed and analyzed using the reversed-phase isolated method. Results are presented in Table 1. HPLC showed the spectrum of drugs from the patients' samples. The chemical component of Rush and Sex Hyper is the same, but they showed different peak retention times. Magic Mushrooms made the varied peaks. Pure White has two chemical components and the two peaks were recognized independently. Pinky made two different peaks in urine. HPLC could be useful in the diagnosis of 'illegal drug' intoxication. However, HPLC has limitations. First, a control drug or a control spectrum is necessary to compare with the spectrum of the patient's sample. Second, HPLC seems to be influenced by additional materials even if they have the same chemical component. Third, we should choose a suitable extract method and column. Because we used acetnitrile not alcohol to extract Magic Mushrooms, HPLC showed many peaks. Finally, urine is not adequate for 'illegal drug' analysis. 2C-I in urine showed different peaks. Serum or gastric juice, before the chemical component is metabolized, should be used.

## P407

## Lethal intoxication with hydrofluoric acid

**C Marx, S Trautmann, M Halank, M Weise**
*University Hospital Carl Gustav Carus, Dresden, Germany*
*Critical Care* 2005, **9(Suppl 1):**P407 (DOI 10.1186/cc3470)

Intoxication with hydrofluoric acid is a very rare but mostly lethal clinical condition. It is mainly caused by dermal exposure, with ingestion extremely rare. Hydrofluoric acid is one of the strongest acids known that has a strong lipophilic ability. Ingestions of more than 20 mg/kg body weight are considered a lethal dose. Even after dermal exposure, the fatal prognosis is caused by severe electrolyte disturbances, especially hypocalcemia.
We report on a 50-year-old female with endogenous depression who swallowed approximately 30 ml hexafluorosilicate (hydrofluoric acid) during a night-time attempt to commit suicide. In the early morning, the woman was found somnolent in a condition of circulatory shock. She complained of severe abdominal pain. She had to be intubated by the emergency doctor and was admitted to the hospital. Physical examination of the mechanically ventilated patient only revealed conjunctival irritation. Laboratory investigations showed severe electrolyte disturbances (hypokalemia, hypocalcemia, hypophosphatemia decreased magnesium levels) as well as severe metabolic acidosis. Within the next few hours, disseminated intravascular coagulation and hyopalbuminemia developed. Serum fluoride levels were 0.099 mmol/l or 1.98 mg/l (normal values 0.0005–0.02 mmol/l or 0.1–0.4 mg/l). Urine fluoride levels were 1.94 mg/l (normal values <1.0 mg/l). Gastroscopy showed necrotic gastric mucosa without signs of bleeding. Topical instillation of calcium was not performed due to the long time interval from burn to treatment but intravenous calciumgluconate was substituted immediately.
Despite fluid resuscitation, correction of the electrolyte abnormalities, stabilisation of coagulation and substitution of albumin, the clinical condition worsened. The patient had to be defibrillated due to ventricular fibrillation about 30 times. Later on, these episodes of ventricular fibrillation were becoming less responsive to defibrillation although the electrolyte threshold had already been corrected. After 12 hours, the patient died under cardiopulmonary resuscitation.
On autopsy, severe burns were found in the esophageal and gastric mucosa, hyperemic lesions were seen in the renal tubular system as well as necrotic lesions in the cardiac musculature.
Besides the poor prognosis of a fluoride intoxication in this dosis, the long time interval until treatment could be started seems to be the main reason for the fatal outcome of this case.

**References**

1. Mayer TG, Gross PL: **Fatal systemic fluorosis due to hydrofluoric acid burns.** *Ann Emerg Med* 1985, **14:**149-153.

**Table 1 (abstract P406)**

| Case | Age (years) | Sex | Common name | Component | HPLC spectrum | Peak time (min) |
|---|---|---|---|---|---|---|
| 1 | 26 | Male | Rush | 5-MEO-DIPT | Recognized | 7.6 |
| 2 | 24 | Female | Magic Mushrooms | Psilocin | Recognized | Many peaks |
| 3 | 20 | Male | Sex Hyper | 5-MEO-DIPT | Recognized | 11.1 |
| 4 | 24 | Male | Pure White | 2CT-2, 2CT-7 | Recognized | 11.3, 12.4 |
| 5 | 28 | Male | Sex Hyper | 5-MEO-DIPT | Recognized | 11.1 |
| 6 | 17 | Male | Pinky | 2C-I | Recognized | 10.6, 10.8 |

2. Mullett T, Zoeller T, Bingham H, Pepine CJ, Prida XE, Castenholz R, Kirby R: **Fatal hydrofluoric acid cutaneous exposure with refractory ventricular fibrillation.** *J Burn Care Rehabil* 1987, **8:**216-219.
3. Chan BS, Duggin GG: **Survival after a massive hydrofluoric acid ingestion.** *J Toxicol Clin Toxicol* 1997, **35:**307-309.

## P408

### Dispersion of the corrected QT interval in acute carbon monoxide poisoning

**B Yelken, B Tanriverdi, F Cetinbas**
*Osmangazi University Medical Faculty, Eskisehir, Turkey*
*Critical Care* 2005, **9(Suppl 1):**P408 (DOI 10.1186/cc3471)

Carbon monoxide (CO) poisoning is known to cause myocardial toxicity and life-threatening arrhythmias. Corrected QT dispersion (QTdc) of the ECG is an indirect measure of heterogeneity of ventricular repolarisation, which may contribute to ventricular arrhythmias.
The aim of the study was to evaluate the relationship between the carboxyhemoglobin (COHb) level and QTdc during carbon monoxide poisoning.
This study was prospectively performed in 104 patients who diagnosed CO intoxication. Patients were assigned to two groups according to COHb levels < 25% (Group I, $n = 32$) or COHb > 25% (Group II, $n = 72$). In each ECG lead, the QT interval and QRS duration were measured in the two groups and corrected for heart rate (QTc) using Bazett's formula (QT/RR1/2). QTdc is then the difference between the leads with the shortest and longest QTc intervals. Measurement of QT intervals were calculated at admission and in 24-hour and 48-hour ECGs after admission. Cardiac enzymes were measured at each stage. The myocardial perfusion after exercise and at rest 4 hours after exercise were determined in all patients 1 week after admission.
QT, QTc and QTd intervals were not significantly different in both of groups each stage whereas the values of the QTdc after 24 hours were significantly greater than QTdc at admission in Group II but not in Group I. Comparison of QTdc for the two groups demonstrated significant differences after 24 hours ($P < 0.05$) (Table 1). Plasma creatinine phosphokinase (CPK) and CPK-MB levels at admission, and 24 and 48 hours later in Group II were significantly higher than the other group ($P < 0.05$). Seven patients in Group I and 23 patients in Group II had an extent of myocardial ischemia on scintigraphy.

**Table 1**

| | Group I (COHb < 25%) | Group II (COHb > 25%) | *P* value |
|---|---|---|---|
| QTdc interval | | | |
| Admission | 95.68 ± 5.9 | 93.90 ± 7.8 | 0.44 |
| 24 hours after admission | 90.55 ± 5.5 | 105.89 ± 12.1 | 0.005 |
| 48 hours after admission | 90.30 ± 9.9 | 85.93 ± 11.7 | 0.32 |
| QTc interval | | | |
| Admission | 450.49 ± 6.7 | 455.41 ± 4.35 | 0.13 |
| 24 hours after admission | 429.29 ± 6.0 | 439.61 ± 6.9 | 0,69 |
| 48 hours after admission | 431.61 ± 6.9 | 422.69 ± 8.1 | 0.68 |

The reduced threshold for arrhythmias in CO poisoning may be due to inhomogeneous repolarization of ventricles, assessed by QTdc. Measuring QTdc for monitoring after CO poisoning may be suggestive of the potential danger of high levels of COHb to cardiac-disabled individuals

## P409

### A new electronic urine meter (UREXACT) is more accurate in measuring urine output than the standard Urinometer: a comparative study

**M Hersch, L Kanter**
*Shaare Zedek Medical Centre, Jerusalem, Israel*
*Critical Care* 2005, **9(Suppl 1):**P409 (DOI 10.1186/cc3472)

**Introduction** Urine output (UO) measurement is an essential part of fluid balance management while caring for critically ill patients. Moreover, it is the most reliable reflection of organ perfusion. The traditional way of monitoring UO is by visual hourly readings of the amount of urine accumulated in a 'scaled container' = Urinometer. These vary according to nurses' technical and visual inaccuracies.
**Hypothesis** An electronic flow meter (Urexact) will measure UO in a much more accurate, efficient, user-friendly and 'hands-off' manner than the nurses/Urinometer.
**Methods** Adult ICU patients who were expected to be in the ICU ≥ 24 hours were enrolled. UO was measured hourly by the standard Urinometer (nurse) or by the Urexact, for 10 hours each. Hourly urine volume was validated in both techniques by a 'measuring cylinder' operated by a laboratory technician (accuracy of ± 1 ml). Medical personnel completed a questionnaire regarding satisfaction using the Urexact.
**Results** Eighty percent of the Urexact measurements were accurate within ± 10% of the actual 'cylinder measurement' versus only 65% of the Urinometer measurements. Eighty-six percent of

**Figure 1 (abstract P409)**

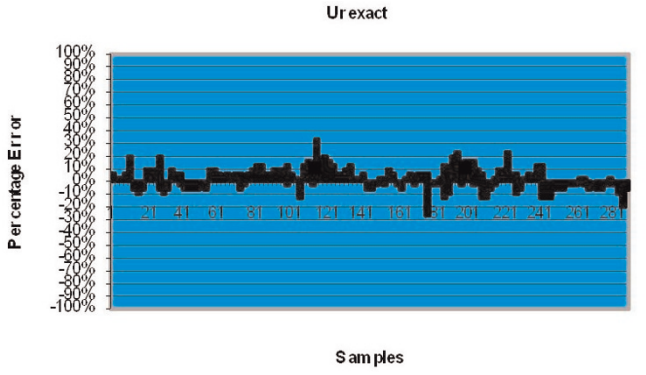
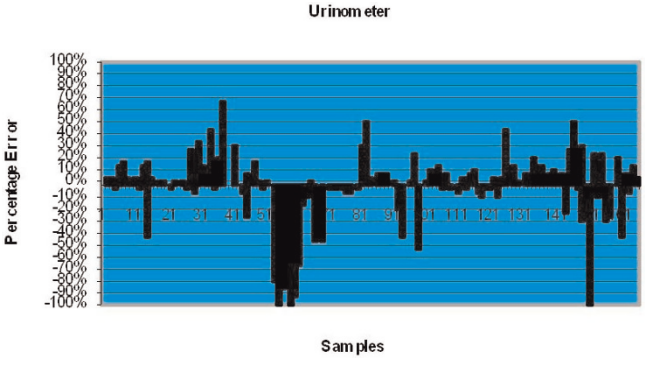



**Figure 2 (abstract P409)**



the nurses graded the Urexact as a very-easy/easy instrument to operate reliably, while saving time and avoiding urine contact.
**Conclusions** Urexact is an accurate, easy-to-use and time-saving device, compared with the standard Urinometer. It is well accepted by the ICU staff and allows them to measure UO without urine contact. It has the potential to allow for fully computerized real-time management of fluid balance.

**References**
1. Bosman RJ, Rood E, Oudemans-van Straaten HM, *et al.*: **Intensive care information system reduces documentation time of the nurses after cardiothoracic surgery.** *Intensive Care Med* 2003, **29:**83-90.
2. Paltiel O, Gordon L, Berg D, *et al.*: **Effect of a computerized alert on the management of hypokalemia in hospitalized patients.** *Arch Intern Med* 2003, **163:**200-204.

## P410

### A computerized alert system for hypokalemia can decrease time to treatment

**E Segal, L Toderis, D Livingstone, A Axel, Y Waheeb, B Lavie, A Perel**
*Sheba Medical Center, Ramat Gan, Israel*
*Critical Care* 2005, **9(Suppl 1):**P410 (DOI 10.1186/cc3473)

**Introduction** Computerized systems are becoming increasingly important in critical care. Systems can record physiological data automatically, leading to improved charting and reducing time requirement for charting by nurses [1], and can perhaps impact favorably on clinical decisions.
An additional potential advantage of computerized systems is the ability to alert clinicians to various clinical occurrences, thus improving care. This has been shown regarding hypokalemia in a hospital-wide computerized system [2]. We examined the impact of a computerized alert for a low potassium level in our general ICU. We hypothesized that an alert provided by the computerized system will reduce the response time of the clinical staff to hypokalemia.
**Methods** The general ICU at the Sheba Medical Center is a 12-bed ICU in a 1600-bed tertiary hospital. Three years ago a computerized system was implemented (Metavision; IMDsoft Ltd, Israel). The system receives and charts data automatically. The system has an 'Event Manager' module that enables clinicians to determine various indicators that will trigger an alert to the staff. We created an alert that responds to a low potassium level by presenting a message at the patient workstation indicating that a low potassium measurement has been detected and consideration should be given for supplemental potassium. The clinical staff received a general update regarding the implementation of the event without specific training. The event was introduced almost 2 years after the staff had been working with the computerized system. We retrospectively looked at the time to treat (TTT) from measurement of a potassium level lower than 2.9 meq/l during the year before the event was implemented (Before event) and compared this with the time period after the event was implemented (After event). There was a statistically significant reduction in the time to treat between the two time periods (Table 1).

**Table 1**

| | *n* | Mean (min) | Median (min) |
|---|---|---|---|
| Before event | 542 | 85 | 52 |
| After event | 423 | 70 | 34 |
| | | $P < 0.01$ | $P < 0.0001$ |

**Discussion** A computerized alert that notifies clinicians of a low potassium measurement can decrease the time to recognition and treatment of hypokalemia, and thus improve care.
**Conclusions** Computerized alerts regarding laboratory results may impact clinical care.
**Acknowledgements** ES and AP are consultants to IMDsoft.

## P411

### Acetazolamide-mediated decrease in strong ion difference accounts for the correction of metabolic alkalosis in intensive care unit patients

**P Pickkers, M Moviat, H Van der Hoeven**
*University Hospital Nijmegen, The Netherlands*
*Critical Care* 2005, **9(Suppl 1):**P411 (DOI 10.1186/cc3474)

**Introduction** Metabolic alkalosis is a well-known acid–base derangement in the ICU. Treatment with the carbonic anhydrase inhibitor acetazolamide is indicated in selected cases. According to the quantitative physicochemical approach described by Stewart, correction of serum pH due to carbonic anhydrase inhibition in the proximal tubule cannot be explained by excretion of bicarbonate. pH is exclusively mediated by three independent variables: $pCO_2$, total concentration of weak acids, and the difference between dissociated anions and cations (SID). We therefore studied the mechanism of action of acetazolamide in critically ill patients with a metabolic alkalosis according to the Stewart approach.
**Methods** The study was approved by the local ethics committee and the need for informed consent waived. Fifteen consecutive ICU patients with metabolic alkalosis (pH > 7.48 and $HCO_3$ > 28 mmol/l) were treated with a single administration of 500 mg acetazolamide intravenously. Serum levels of strong ions, creatinine, lactate, weak acids, pH and $pCO_2$ were measured at 0, 12, 24, 48 and 72 hours. Main strong ions of the urine (sodium, chloride and potassium) and pH were measured at 0, 3, 6, 12, 24, 48 and 72 hours. Strong ion difference (SID), strong ion gap (SIG) and the Na–Cl effect were calculated. Effects of acetazolamide were analyzed by comparing baseline variables and the time-dependent changes by one-way analysis of variance for repeated measures.
**Results** Eighty-seven percent of patients were mechanically ventilated and 47% were treated with diuretics. Ventilator settings and diuretic dose were not changed during the study period. Mean APACHE II score was 21 (range 12–30) and hospital mortality was 20% (SMR 0.57). Correction of serum pH (7.49 ± 0.01 to 7.46 ± 0.01; $P = 0.001$) was maximal at 24 hours and sustained during the observation period. The parallel decrease in $pCO_2$ was not significant (5.7 ± 0.2 to 5.3 ± 0.2 kPa, $P = 0.08$). Also, there was no significant change in the total concentration of weak acids. Serum SID significantly decreased during the observation period (41.5 ± 1.3 to 38.0 ± 1.0 mEq/l, $P = 0.03$) due to an increase in serum chloride (105 ± 1.2 to 110 ± 1.2 mmol/l, $P < 0.0001$). There was a very strong relation between the serum SID and the Na–Cl effect ($R^2 = 0.99$, $P = < 0.001$) The decrease in serum SID was explained by a significant increase in the urinary excretion of sodium without chloride in the first 24 hours (urinary [Na]/[Cl] 1.3 ± 0.3 to 2.5 ± 0.5, $P = 0.02$).
**Conclusions** A single dose of acetazolamide effectively corrects metabolic alkalosis in critically ill patients by decreasing the serum SID. This effect is completely explained by the increased renal excretion ratio of sodium/chloride, resulting in an increase in serum chloride.

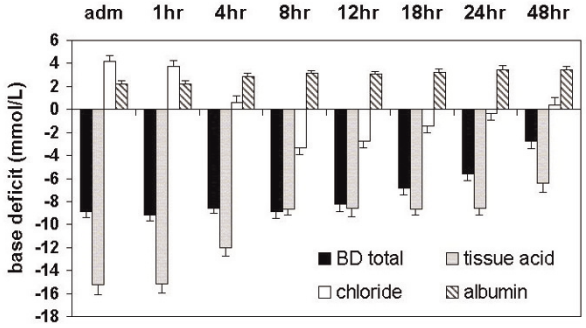
## P412

### Acid–base changes in meningococcal sepsis revealed by partitioning the base deficit

**S Tibby, E O'Dell, A Durward, I Murdoch**
*Guy's Hospital, London, UK*
*Critical Care* 2005, **9(Suppl 1):**P412 (DOI 10.1186/cc3475)

**Introduction** Base deficit (BD) quantifies a metabolic acidosis without defining aetiology. Factors contributing to a metabolic acidosis include lactic acid and unmeasured anions (together known as tissue acid), hyperchloraemia and plasma albumin concentration. An equation exists to quantify the effect of albumin on BD; we have recently derived a similar equation for the effect of chloride. After partitioning the BD for these factors, the residual BD should reflect the contribution from tissue acid.
**Aim** In patients with meningococcal sepsis, we aimed to: (1) validate this approach by comparing the agreement between tissue acids derived from the partitioned BD with that from the Stewart–Fencl method; and (2) use the partitioned BD to examine the temporal profile of acid base disturbance during the first 48 hours of treatment.
**Methods** Sixty patients admitted to the intensive care unit with meningococcal sepsis over 2 years were studied, median (interquartile) weight 13 kg (10–20), median PIM risk of mortality 10.3% (6–16). Arterial blood was drawn at admission, and at 4, 8, 12, 18, 24 and 48 hours. BD was calculated from a standard algorithm in the blood gas analyser, and tissue acid via the Stewart–Fencl method.
**Results** (1) For the group as a whole, there was a strong association between tissue acid derived from the partitioned BD and the Stewart–Fencl method ($r^2 = 0.83$). (2) A substantial metabolic acidosis was present at admission (mean pH 7.31, standard error of the mean 0.01, mean BD −8.9, standard error of the mean 0.5), which persisted at 24 hours. The admission BD was predominantly due to tissue acid, which was offset by an alkalinising effect of hypochloraemia and hypoalbuminaemia (Fig. 1). By 8 hours, chloride was now exhibiting an acidifying effect, which was related to the amount of chloride administered in the resuscitation fluids ($r^2 = 0.41$).
**Conclusion** The partitioned BD provides an accurate measure of tissue acid, and can be used to identify changes in the cause of a metabolic acidosis over time.

**Figure 1 (abstract P412)**




## P413

### Peripheral oedema may not reflect capillary leak in severe sepsis: pilot study

**J Tóth, T Szakmány, Z Molnár**
*University of Pécs, Hungary*
*Critical Care* 2005, **9(Suppl 1):**P413 (DOI 10.1186/cc3476)

**Objectives** Whether systemic capillary leak can be monitored or whether it exists at all remains controversial [1]. The aim of this study was to investigate the origin of peripheral oedema in patients with severe sepsis.
**Materials and methods** Ten patients fulfilling the severe sepsis criteria [2], requiring mechanical ventilation, and having a high (> 2 mm) oedema score were recruited [3], and observed daily, for 3 days. Subcutaneous oedema fluid (5 ml) was drained from the patients' back of the hand using a special, perforated 20G intravenous cannula once a day. At the same time arterial blood and urine were collected (5 and 10 ml, respectively). From oedema and blood samples total protein, albumin and inflammatory markers (PCT, CRP, tumour necrosis factor alpha, IL-6, IL-8), and from urine microalbuminuria (MCR) levels were determined. Oedema was considered due to capillary leak if the oedema protein (TPoe)/serum total protein (TPs) ratio ≥ 0.65, and hydrostatic if < 0.65 [4]. Data are presented as the mean ± standard deviation, or the median and interquartile range (IQR) according to the data distribution.
**Results** In addition to clinical signs, all patients proved to be septic as indicated by high inflammatory marker levels (Table 1). Increased capillary leak was suggested by high oedema score, 3.3 ± 0.6 mm, and elevated MCR. However, the TPoe/TPs ratio was 0.21 ± 0.16, indicating mainly hydrostatic forces as a reason for peripheral oedema

**Table 1**

| | Median | IQR | Normal |
|---|---|---|---|
| PCT (ng/ml) | 8.0 | 1.0–23.3 | < 0.5 |
| CRP (mg/l) | 135 | 89–234 | <10 |
| Tumour necrosis factor alpha (pg/ml) | 14.2 | 6.1–43.2 | < 8.1 |
| IL-8 (pg/ml) | 49.0 | 22.7–196.0 | < 2.0 |
| MCR (mg/mmol) | 5.3 | 3.0–12.0 | < 4.28 |

**Discussion** To our knowledge this is one of the first studies to address the question of the origin of the oedema fluid in severe sepsis. The low TPoe/TPs ratio found indicates mainly hydrostatic forces in oedema formation. These preliminary results suggest that, despite evidence of severe sepsis, the diagnosis of 'increased capillary leak' cannot be made on the basis of the clinical signs of severe peripheral oedema.

**References**

1. Molnar Z, Szakmany T, Heigl P: *Intensive Care Med* 2003, **29:**391-395.
2. ACCP/SCCM Consensus Conference: *Crit Care Med* 1992, **20:**864-875.
3. Diskin CJ, Stokes TJ, Dansby LM, *et al.*: *BMJ* 1999, **318:**1610-1613.
4. Sue RD, Matthay MA, Ware LB: Intensive *Care Med* 2004, **30:**1921-1926.

## P414

### Comparative evaluation of extracellular mass and body cell mass between patients with SIRS and severe sepsis by bioelectrical impedance analysis

**G Tsoros[1], M Paraschos[1], M Michail[1], A Amygdalou[1], M Moukas[1], M Vassiliou[2], C Mandragos[1]**
*[1]Red Cross Hospital of Athens, Greece; [2]Pneumonology Department, School of Medicine, University of Ioannina, Greece*
*Critical Care* 2005, **9(Suppl 1):**P414 (DOI 10.1186/cc3477)

**Introduction** The present study compares the changes of extracellular mass (ECM) and body cell mass (BCM) in patients with SIRS and severe sepsis with the aid of bioelectrical impedance analysis.
**Methods** In the study, 32 mechanically ventilated SIRS patients were included. The total body water balance and nitrogen balance (NB) were evaluated everyday. ECM and BCM were measured in kilograms, by bioelectrical impedance analysis at the first and 10th ICU hospitalisation day. On the second measurement, 12 patients (SIRS group) remained in SIRS with stable health status or improvement, while 18 patients had severe sepsis (SEPSIS group). Differences between the first and second measurement were expressed as ΔECM and ΔBCM. Alterations of all studied parameters were compared between the two groups with the student paired *t* test ($P < 0.05$).
**Results** BCM was significantly reduced from 23.7 ± 7.21 to 19.0 ± 7.01 ($P = 0.048$). The reduction in the SEPSIS group was insignificant (from 21.8 ± 6.28 to 20.3 ± 5.74, $P = 0.252$). The difference between the corresponding changes was not significant ($P = 0.2180$).
ECM decreased non-significantly in the SIRS group (from 36.6 ± 9.91 to 35.3 ± 7.88, $P = 0.666$). On the contrary, ECM increased significantly in the SEPSIS group (from 37.7 ± 11.94 to 49.2 ± 13.09, $P < 0.0001$). Changes of ECM differed significantly between the two groups ($P = 0.0011$). The total body water balance in the SIRS group (602.9 ± 2938.85) was significantly lower than in the SEPSIS group (12,779.4 ± 8025.75) ($P < 0.0001$). The NB was negative in both groups (SIRS: 1.5 ± 3.74; SEPSIS: 4.3 ± 4.23), but their difference was not significant ($P = 0.7308$).
**Conclusions** The present study shows that BCM and NB follow a similar reduction pattern in both groups, although it is not correlated. This finding could be related to the multivariate influence on BCM (catabolism, immobilization, medication). It seems that ECM changes reflect the process of the disease since it decreased in the rather stable SIRS group and increased in the deteriorating SEPSIS group.

## P415

### Strong ion acid–base abnormality and lactate:pyruvate ratio in children following cardiopulmonary bypass

**M Hatherill, M Salie, Z Waggie, J Lawrenson, J Hewitson, L Reynolds, A Argent**
*Red Cross Children's Hospital, Cape Town, South Africa*
*Critical Care* 2005, **9(Suppl 1):**P415 (DOI 10.1186/cc3478)

**Objectives** To describe post-cardiopulmonary bypass (post-CPB) acid–base derangement in terms of the Fencl–Stewart strong ion approach and the lactate:pyruvate ratio (LPR).
**Methods** A prospective observational study set in the PICU of a university hospital. Arterial blood gas, serum lactate, pyruvate, and electrolytes were measured on admission to the PICU following cardiac surgery with CPB. LPR, corrected chloride (cCl = 140 × Cl/Na), and unmeasured anions or cations (strong ion gap) were calculated using modified Fencl–Stewart equations. CPB time, percent predicted mortality (PIM I), PICU mortality, and duration of: ventilation; inotropic support; and PICU stay were recorded. Data are reported as the median (range), or *n* (%), and are analysed by Mann–Whitney and Fisher's Exact tests. Ninety-four children, median age 51 months (0.03–166), median weight 14 kg (2.1–50), were enrolled.
**Results** Surgery was performed for cyanotic heart disease in 41 children (44%) and acyanotic heart disease in 53 children (56%). Median CPB time was 80 min (17–232). One child died (PICU mortality 1%). Predicted mortality was 2% (SMR 0.50). The median pH was 7.38 (7.17–7.61). Of 69 children with standard bicarbonate < 22 mmol/l, the primary factor causing metabolic acidosis was elevated cCl in 32 patients (46%), lactate in three patients (4%), unmeasured anions in two patients (4%), and mixed in 32 patients (46%). The median base excess (BE) was −5.0 meq/l (−12.9 to −2.5), with chloride effect of −10.8 meq/l (−24 to +1.2), free water effect of −0.6 meq/l (−3.3 to +1.8), albumin effect of +3.5 meq/l (−0.6 to +6.8), and unmeasured cation effect of +3.7 meq/l (−10.7 to +17). The median cCl was 113 mmol/l (101–126). Hyperchloraemia (cCl >110 mmol/l) occurred in 66 children (70%) and was negatively associated with use of adrenaline by infusion ($P = 0.005$). Median lactate was 1.9 mmol/l (0.7–9.1) and hyperlactataemia (> 2 mmol/l) occurred in 41 children (44%). The median LPR was 18.8 (5.4–35) and LPR was raised (> 20) in 42 children (45%). Hyperlactataemia plus raised LPR was associated with use of adrenaline by infusion ($P = 0.0009$), CPB time ($P = 0.04$), percent predicted mortality ($P = 0.05$) and PICU stay ($P = 0.03$). Median albumin was 30 g/l (16-44) and hypoalbuminaemia (< 35 g/l) occurred in 81 children (86%). The median calculated strong ion gap was −3.8 mmol/l (−18.4 to +9.1) (i.e. unmeasured cation predominance).
**Conclusion** In this group of children with low mortality post-CPB, hyperchloraemia was primarily responsible for metabolic acidosis, although both hyperlactataemia and raised LPR were common. Both hypoalbuminaemia and unmeasured cations limited the magnitude of the base deficit.

## P416

### Magnesium at admission: is it an outcome marker in the critically ill patients?

**M Passakiotou, C Lampiri, E Kopatzidis, N Sounidakis, M Asimaki, N Gritsi-Gerogianni**
*Intensive Care Unit, Hippokration Hospital, Thessaloniki, Greece*
*Critical Care* 2005, **9(Suppl 1):**P416 (DOI 10.1186/cc3479)

**Introduction** Magnesium (Mg) is the fifth most common cation in the body, considered, however, as the 'forgotten cation' in clinical practice [1]. Mg deficiency is rather common in critically ill patients and recent studies found that reductions in total serum Mg at admission are associated with increased mortality [2]. Loss of Mg can lead to vasoconstriction, especially of cerebral and coronary arteries, while Mg appears to play a role in the scavenging of free radicals and the prevention of reperfusion injury [3].
**Aim** An observational study on the evaluation of total serum Mg in a tertiary 10-bed intensive care unit.
**Patients** Ninety-five patients admitted to the ICU over a 6-month period: 30 polytrauma, 11 COPD, 12 stroke, nine liver transplantation, 13 postoperative, five eclampsia and 15 miscellaneous. Mean age: 43.2 years, length of stay: 9.2 days, APACHE II score: 11.3 ± 7.5, mortality: 34%.
**Measurements and results** Total serum Mg, calcium, phosphorus and proteins were measured at admission and then every day until discharge from the ICU. At admission, 15/30 polytrauma, 6/13

postoperative, 4/12 stroke, 5/5 eclampsia, 8/9 liver transplantation, 2/11 COPD and 5/15 miscellaneous patients had <1.3 mg/dl total serum Mg. Calcium and phosphorus deficiency was not remarkable in any of the groups, while total proteins were found in relatively low levels (< 3.5 mg/dl) in polytrauma and postoperative patients. Low APACHE II score and negative outcome had a relative correlation with low Mg levels in all groups, whereas Mg replacement had not affected patients' outcome. ICU length of stay had no correlation to low Mg levels at admission.

**Conclusion** Hypomagnesemia at admission is relatively associated with a worse prognosis, considering, however, that other major factors (e.g. sepsis, MODS) play the first role in critically ill patients' outcome.

**References**

1. Elin RJ: **Magnesium: the fifth but forgotten electrolyte.** *Clin Chem* 1994, **102:**616-622.
2. Rubeiz GJ, Thill-Baharozian M: **Association of hypomagnesemia and mortality in acutely ill medical patients.** *Crit Care Med* 1993, **21:**203-209.
3. Noronha JL, Matuchak GM: **Magnesium in critical illness: metabolism, assessment and treatment.** *Intensive Care Med* 2002, **28:**667-679.